

A SHORT REVIEW ON POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Polycystic ovary syndrome (PCOS) is said to be the most common endocrine disorder in women of reproductive age with a heterogeneous presentation, which includes hyperandrogenism and ovulatory dysfunction. PCOS usually has a peripubertal onset; the present review discusses the causes, complications, risk factors, diagnosis, and treatment.

Keywords: Polycystic ovary syndrome, Hyperandrogenism, Treatment.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder. As one of the leading causes of anovulatory infertility, it is believed that 5-10% of the reproductive-aged female population is living with PCOS. First recognized by Stein and Leventhal, in 1935, PCOS is characterized by the presence of polycystic ovaries, menstrual irregularities, and clinical/biochemical hyperandrogenism. The development of PCOS has been linked to hereditary and environmental factors including genetics, insulin resistance, obesity, and birth weight. The presence of PCOS is associated with an increased prevalence of adverse health conditions such as the metabolic syndrome, cardiovascular disease, and Type II diabetes mellitus. Insulin resistance is believed to play a key role in the development of PCOS and the development of related conditions. In the past few years, research has been done to better understand the mechanisms behind the development PCOS and the impact it has on the female body, particularly in relationship to insulin resistance.

DEFINITION

PCOS is a common endocrine system disorder among women of reproductive age. Women with PCOS may have enlarged ovaries that contain small collections of fluid called follicles located in ovaries and have abnormalities in the metabolism of androgens and estrogen (Fig. 1).

TYPES OF PCOS

- Type 1 PCOS: (a) Insulin-resistant PCOS
(b) Non-insulin-resistant types of PCOS
- Type 2 PCOS: Pill-induced PCOS or post-pill PCOS
- Type 3 PCOS: Inflammatory PCOS
- Type 4 PCOS: Hidden-cause PCOS

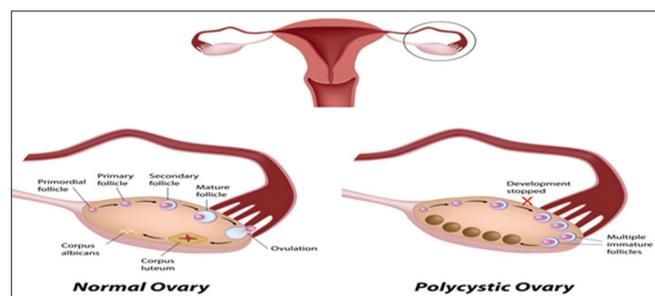


Fig. 1: Polycystic ovary syndrome

Type 1 PCOS

Insulin-resistant PCOS

In this type of PCOS, insulin resistance and leptin resistance will occur due to improper signaling from these metabolic hormones inhibit ovulation and cause the ovaries to produce testosterone. It is a problem with the metabolic hormones that is the main cause of weight gain. The symptoms of excessive testosterone such as acne and facial hair will improve when insulin and leptin sensitivity improve.

Causes of Insulin resistance and Type 1 PCOS:

- Leptin resistance
- Too much sugar
- Smoking
- Hormone-disrupting toxins such as Bisphenol A
- Birth control pill.

Non-insulin-resistant types of PCOS

The ultrasound may show multiple, undeveloped follicles. Luteinizing hormone (LH) may be elevated, and periods do not occur regularly. Testosterone may be high or normal. If testosterone is normal, the acne and facial hair exist because estrogen is too low (compared to testosterone). Body weight can be normal. In insulin-resistant type, the ovaries were prevented from ovulating because of insulin. In other types of PCOS, the ovaries are prevented from ovulating because of unknown reason.

Type 2 PCOS

Pill-induced PCOS or post-pill PCOS

The birth control pill suppresses ovulation. For most women that are a temporary effect and ovulation will usually resume fairly soon after the pill is stopped. However, for some women, ovulation-suppression can persist for months or even years. During that time, it is not unusual to be given the diagnosis of PCOS. It is the second most common type of PCOS.

Type 3 PCOS

Inflammatory PCOS

Inflammation or chronic immune activation results from stress, environmental toxins, intestinal permeability, and inflammatory foods such as gluten or A1 casein. Inflammation is a problem for PCOS because it impedes ovulation, disrupts hormone receptors, and stimulates adrenal androgens such as dehydroepiandrosterone and androstenedione.

Type 4 PCOS

Hidden-cause PCOS

There is one simple thing that is blocking ovulation. Once that single thing is addressed, this type of PCOS resolves very quickly, usually within 3-4 months. Common hidden-causes of PCOS include:

- Soy, because it is anti-estrogen and can block ovulation in some women
- Thyroid disease because your ovaries need T3 thyroid hormone
- Vegetarian diet because it causes zinc deficiency, and ovaries need zinc
- Iodine deficiency because ovaries need iodine
- Artificial sweeteners because they impair insulin and leptin signaling
- Too little starch in diet because the hormonal system needs gentle carbs.

EPIDEMIOLOGY

The exact prevalence of PCOS is not known as the syndrome is not defined precisely. Globally, prevalence estimates of PCOS are highly variable, ranging from 2.2% to as high as 26%. The estimated prevalence in women of reproductive age is 5-10%. Under the new criteria (Rotterdam, 2003), the prevalence among the general female population will raise up to 10%.

ETHIOLOGY/CAUSES

The exact cause of PCOS is unknown, but it is related to abnormal hormone levels.

Resistance to insulin

Insulin is a hormone produced by the pancreas to control the amount of sugar in the blood. It helps move glucose from the blood into cells, where it is broken down to produce energy. Insulin resistance means the body's tissues are resistant to the effects of insulin. The body, therefore, has to produce extra insulin to compensate. High levels of insulin cause the ovaries to produce too much testosterone hormone, which interferes with the development of the follicles (the sacs in the ovaries where eggs develop) and prevents normal ovulation. Insulin resistance can also lead to weight gain, which can make PCOS symptoms worse because having excess fat causes the body to produce even more insulin.

Hormone imbalance

Many women with PCOS are found to have an imbalance in certain hormones including:

- Raised levels of testosterone: A hormone often thought of as a male hormone, although all women normally produce small amounts of it
- Raised levels of LH: A hormone that stimulates ovulation but may have an abnormal effect on the ovaries if levels are too high
- Low levels of sex hormone-binding globulin: A hormone that helps reduce the effect of testosterone
- Raised levels of prolactin (only in some women with PCOS): A hormone that stimulates the breast glands to produce milk in pregnancy.

The exact reason why these hormonal changes occur is not known. It's been suggested that the problem may start in the ovary itself, in other glands that produce these hormones, or part of the brain that controls their production. The changes may also be caused by the resistance to insulin.

Genetics

The methylenetetrahydrofolate reductase (MTHFR) mutation test is used to detect two relatively common mutations in the MTHFR gene that are associated with elevated levels of homocysteine in the blood and also cause hypothyroidism.

RISK FACTORS

- Diabetes
- 4-7 times higher risk of heart attacks

- High blood pressure or hypertension
- High cholesterol
- High lipids
- Sleep apnea
- Risk of endometrial cancer
- Infertility
- Higher rate of miscarriages
- Higher risk of gestational diabetes
- Obesity which can also lead to low self-esteem and depression
- Liver disease.

PATHOPHYSIOLOGY (FIGS. 2 AND 3)

- Defective sex steroid synthesis and metabolism ovary and adrenal gland contribute to steroid production through a similar pathway
- Increased LH, adrenocorticotropic hormone, and insulin increase production of androgens.

Hyperandrogenism results

- Insulin resistance
 - Found in both lean and obese women
 - Post-binding defect in insulin-receptor signaling
 - Insulin sensitivity is selective and tissue dependent
 - Androgen production and/or beta cell defects may exacerbate insulin resistance
 - Strong predictor of sleep apnea for PCOS patients.
- Hyperinsulinemia results
 - Compensatory increase in insulin secretion secondary to peripheral insulin resistance.

SIGNS AND SYMPTOMS

The major features of PCOS include menstrual dysfunction, anovulation, and signs of hyperandrogenism 70% (hirsutism, acne, and male pattern alopecia), anovulation (70-75%) (usually chronic -presents as oligomenorrhea and/or amenorrhea, infertility, and recurrent miscarriages common).

Other signs and symptoms of PCOS may include the following:

- Obesity (50%)
 - Abdominal obesity
 - Waist to hip ratio >0.8.
- Diabetes due to insulin resistance (75%)
- Obstructive sleep apnea
- Oligomenorrhea/amenorrhea
- Infertility/first-trimester miscarriage
- Acanthosis nigricans.

COMPLICATIONS

- Type 2 diabetes
- High blood pressure
- Cholesterol and lipid abnormalities such as elevated triglycerides or low high-density lipoprotein cholesterol, the "good" cholesterol
- Metabolic syndrome – a cluster of signs and symptoms that indicate a significantly increased risk of cardiovascular disease
- Nonalcoholic steatohepatitis – a severe liver inflammation caused by fat accumulation in the liver
- Infertility
- Sleep apnea
- Depression and anxiety
- Abnormal uterine bleeding
- Cancer of the uterine lining (endometrial cancer), caused by exposure to continuous high levels of estrogen
- Gestational diabetes or pregnancy-induced high blood pressure.

DIAGNOSIS

On examination, findings in women with PCOS may include the following:

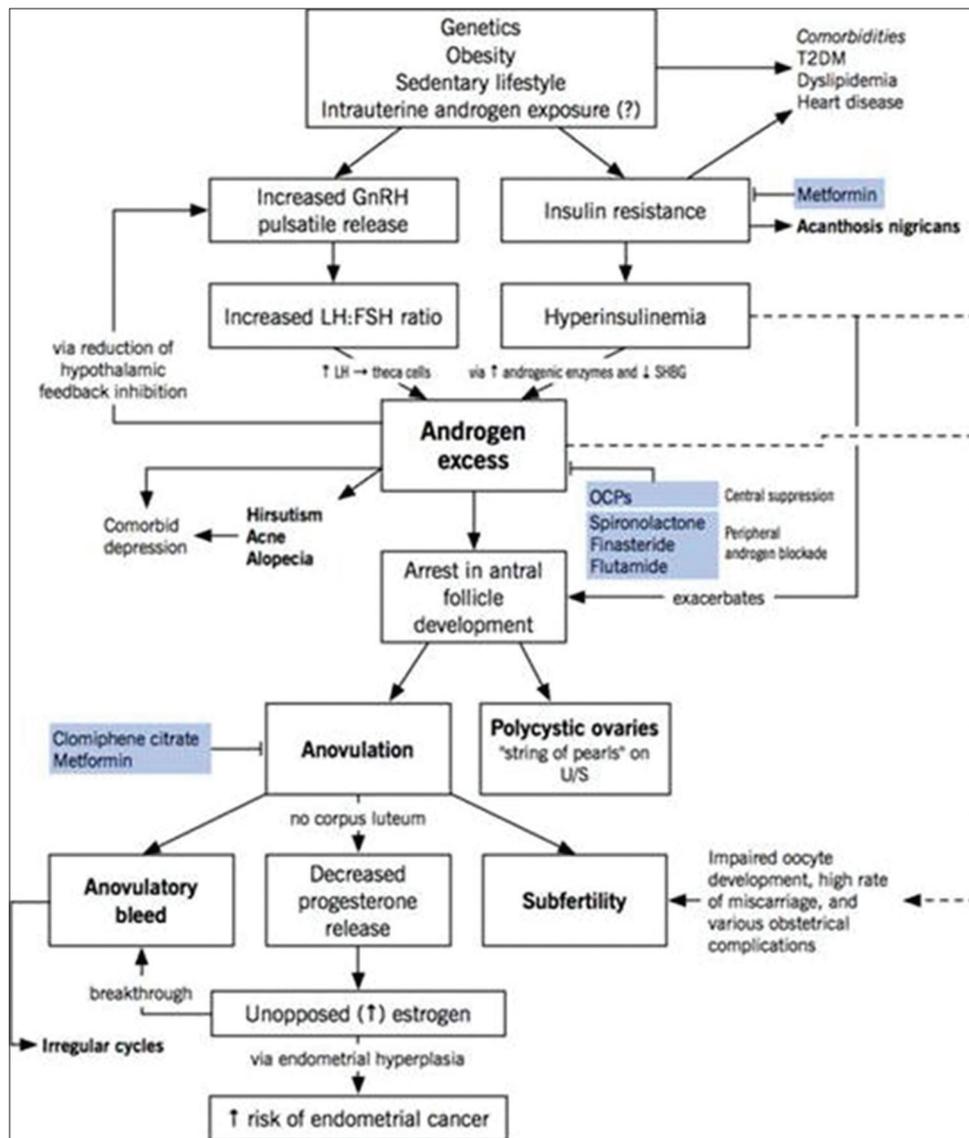


Fig. 2: Pathophysiology of polycystic ovary disease

- Virilizing signs
- Acanthosis nigricans
- Hypertension
- Enlarged ovaries: May or may not be present; evaluate for an ovarian mass.

Testing

Baseline screening laboratory studies for women suspected of having PCOS include the following:

- Thyroid function tests (e.g., thyroid-stimulating hormone, free thyroxine)
- Serum prolactin level
- Total and free testosterone levels
- Free androgen index
- Serum human chorionic gonadotropin level
- Cosyntropin stimulation test
- Serum 17-hydroxyprogesterone level
- Urinary free cortisol and creatinine levels
- Low-dose dexamethasone suppression test
- Serum insulin-like growth factor-1 level
- Other tests used in the evaluation of PCOS include the following:
- Androstenedione level

- Follicle stimulating hormone and LH levels
- Gonadotropin-releasing hormone stimulation testing
- Glucose level
- Insulin level
- Lipid panel.

Imaging tests

The following imaging studies may be used in the evaluation of PCOS (Fig. 4):

- Ovarian ultrasonography, preferably using transvaginal approach
- Pelvic computed tomography scan or magnetic resonance imaging to visualize the adrenals and ovaries.

TREATMENT

Pharmacological treatment

Surgery

Surgical management of PCOS is aimed mainly at restoring ovulation. Various laparoscopic methods include the following (Fig. 5):

- Electrocautery
- Laser drilling.
- Multiple biopsy

Selected treatment options for polycystic ovary syndrome

Drug class (example)	Purpose of therapy	Mechanism of action	Effective dose	Side effects
Combined oral contraceptive (estrogen and progesterone)	Menstrual cyclicity; Hirsutism, acne	Suppresses LH 9 (and FSH) and this ovarian androgen production; increase sex hormone-binding globulin, which decreases free testosterone	One tablet orally daily for 21 (or 24) days, then 7 days (or 4 days) pill-free interval	Breast tenderness, breakthrough bleeding, mood swings, libido changes
Progestins (medroxy-progesterone)	Menstrual cyclicity	Creates withdrawal bleeding by transforming proliferative endometrium	5-10 mg orally daily for 10-14 days every 1-2 months	Breakthrough bleeding, spotting, mood swings
Bigunide (metformin)	Menstrual cyclicity, ovulation induction, hirsutism, acne, insulin lowering	Decreases hepatic glucose production, secondarily reducing insulin levels; may have direct effects on steroidogenesis	1500 mg orally daily in divided doses (up to 2550 mg/d	Gastrointestinal problems, diarrhea, abdominal pain
Thiazolidinediones (pioglitazone)	Menstrual cyclicity, ovulation induction, hirsutism, acne, insulin lowering	Improves insulin sensitivity at target-tissue level (muscle, adipocyte); may have direct effects on steroidogenesis	Pioglitazone: 15-30 mg orally; maximum 45 mg orally	Edema, headache, fatigue, abdominal pain
Antiandrogen (spironolactone)	Hirsutism, acne	Inhibits androgen from binding to androgen receptor	50-100 mg orally twice daily	Hyperkalemia, polymenorrhea, headache, fatigue
Antiestrogen (clomiphene citrate)	Ovulation induction	Increase GnRH secretion, which induces rise in FSH and LH	50 mg orally for 5 days; may increase or 100 mg	Vasomotor symptoms, gastrointestinal problems

FSH: Follicle stimulating hormone, GnRH: Gonadotropin-releasing hormone, LH: Luteinizing hormone

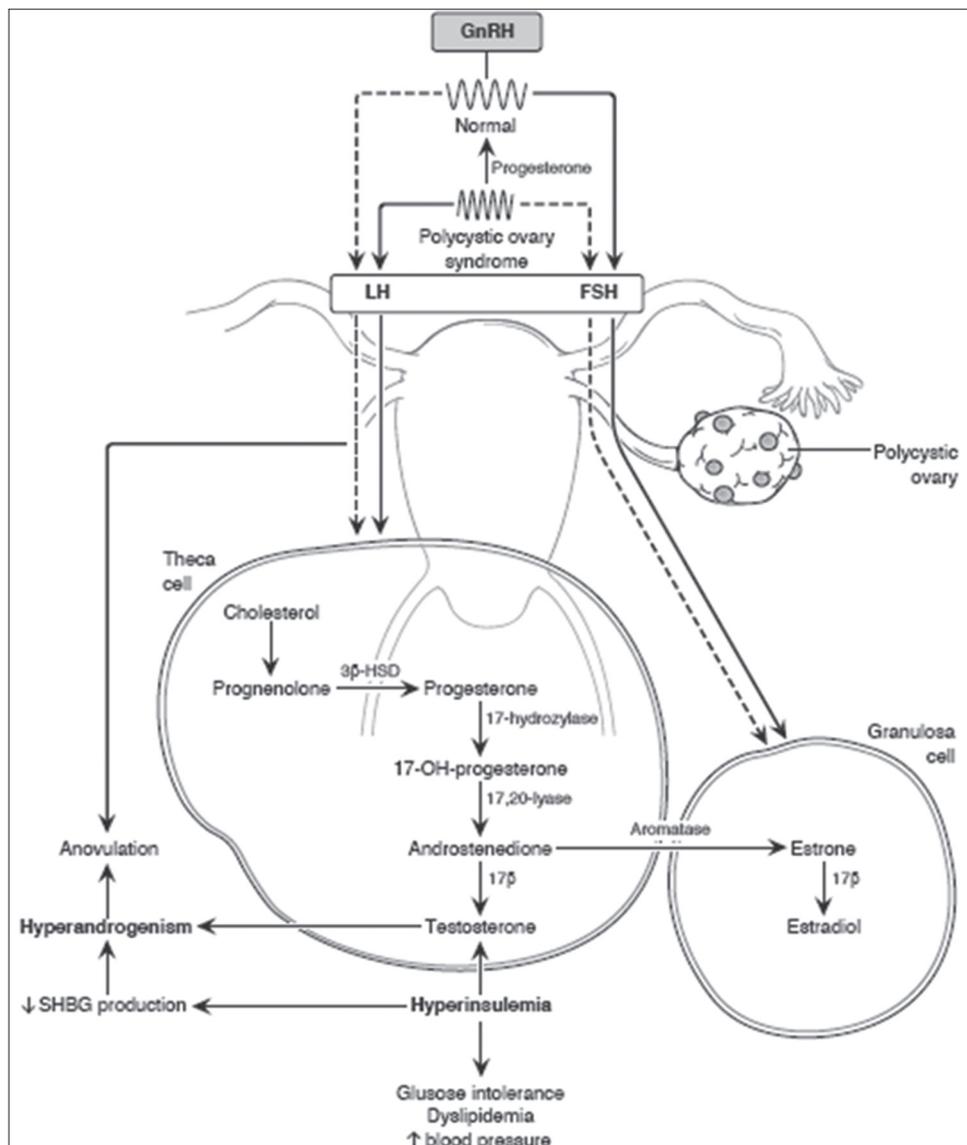


Fig. 3: Relationship of gonadotropin secretion, androgen production, and insulin in polycystic ovary disease

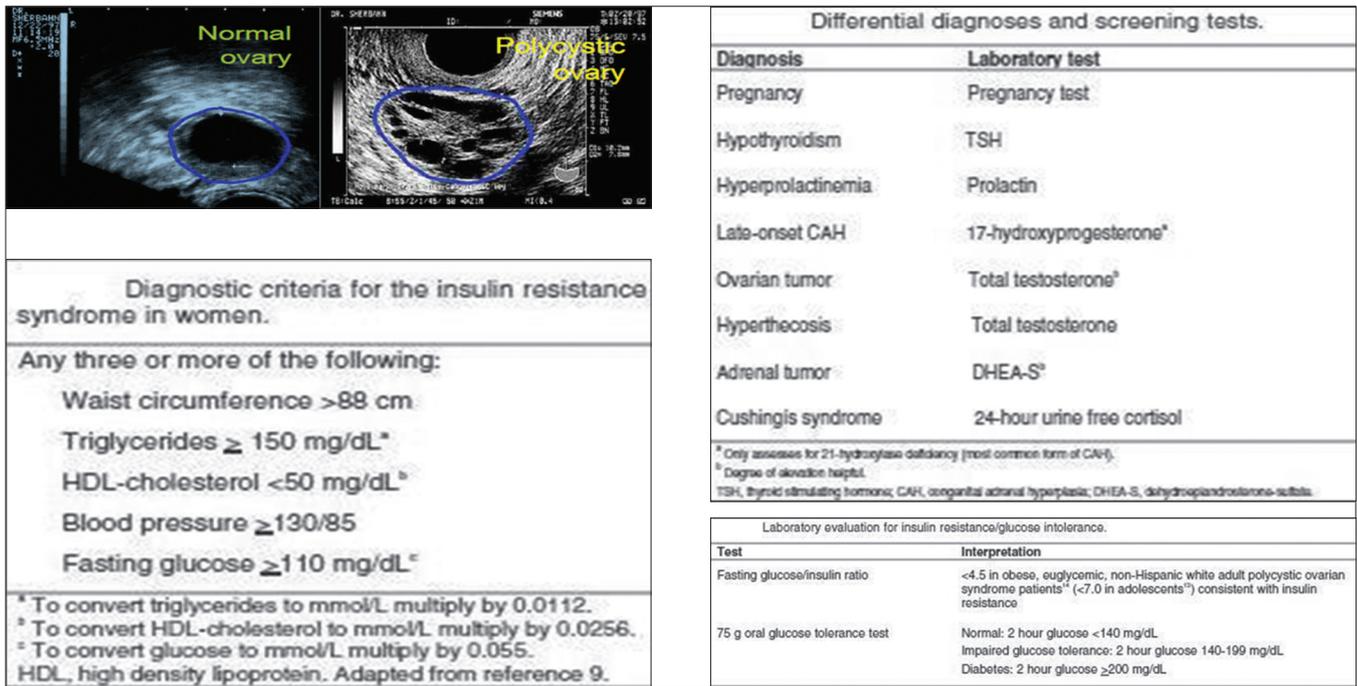


Fig. 4: Ovarian ultrasonography

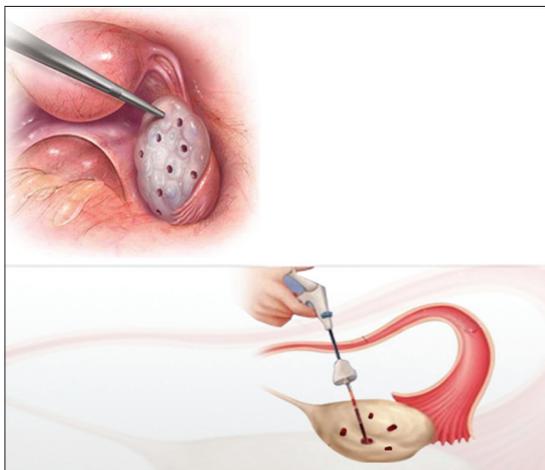


Fig 5: Laser drilling of ovary

Non-pharmacological treatment

- Weight reduction
 - Decreasing body weight 5-10% significantly reduces hyperandrogenism, insulin resistance, and anovulation
 - Incidence of eating disorders higher in PCOS.
- Psychotherapy
- Hair removal
 - Shaving
 - Chemical bleaching and waxing
 - Laser removal.

CONCLUSION

Although PCOS is one of the most common endocrine disorders in women of reproductive age, there is currently no cure for PCOS. For this reason, early diagnosis of the disease based on established criteria is important. With an early diagnosis, it is possible to manage

the manifestations of PCOS. With proper management, obesity and insulin resistance can be controlled for as well as the associated diseases.

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