

## A Review on Current Treatment in Polycystic Ovary Syndrome (PCOS)

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### ABSTRACT

Polycystic ovary syndrome (PCOS) is a chronic, complex and the most common endocrine disorder observed in women of reproductive age. It is called Syndrome because refer to number of symptoms experienced at a same time. There are four types of PCOS, Insulin Resistant PCOS, Post-Pill PCOS, Adrenal PCOS, Inflammatory PCOS. This syndrome is heterogeneous in nature and is characterized by combination of signs and symptoms of androgen excess and ovarian dysfunction. It is a significant public health issue. There is also increased rate of weight gain and prevalence of obesity in PCOS. Increase in severity of the condition causing considerable concern. For these affected and mandating attention to healthy lifestyle. The symptoms of this disorder can be Psychological , reproductive, Menstrual, weight related, dermatological, metabolic and sleep Disorders. Women with Polycystic Ovary Syndrome (PCOS) usually have trouble with their Menstrual cycle due to malfunctioning Ovaries . There is no specific test for PCOS but doctor will consider the symptoms and will complete the physical examination. Also Blood Test and

Transvaginal Ultrasound. This Review is an attempt to summarize the evaluation of diagnosis and current management guidelines and also to look into the future approaches and recent international guidelines for providing and update scientific overview of PCOS.

**Keywords:** Polycystic Ovary Syndrome; PCOS; Hyperandrogenism

### INTRODUCTION

Polycystic ovary syndrome (PCOS) is a chronic, complex and the most common endocrine disorder observed in women of reproductive age, and it is also observed in adolescents. More simply, a hormonal disorder causing enlarged ovaries with small cysts on outer side. It is called Syndrome because refer to number of symptoms experienced at a same time. Also known as Polycystic ovary disease (PCOD) or Hyper androgen Anovulation Syndrome. (HAAS). This is significant public health issue. This syndrome is characterized by a combination of signs and symptoms of androgen excess and ovarian dysfunction

**Types of PCOS :** There are four types of PCOS -

1. <b>Insulin Resistant PCOS</b>	There is higher levels of insulin than normal in the blood. Also known as Hyperinsulinemia.
2. <b>Post-Pill PCOS</b>	Occurs when patient stop taking contraceptive pills
3. <b>Adrenal PCOS</b>	This type of PCOS is due to abnormal stress response and affect around 10 % of diagnosis.
4. <b>Inflammatory PCOS</b>	Chronic inflammation cause the ovary to make excess testosterone result in physical symptoms and issues with ovulation.

Why does it occurs ? Even Doctors are not exactly sure about what are the causes of PCOS, it

is believed to linked to both lifestyle factors and genetics. The majority who have PCOS also have

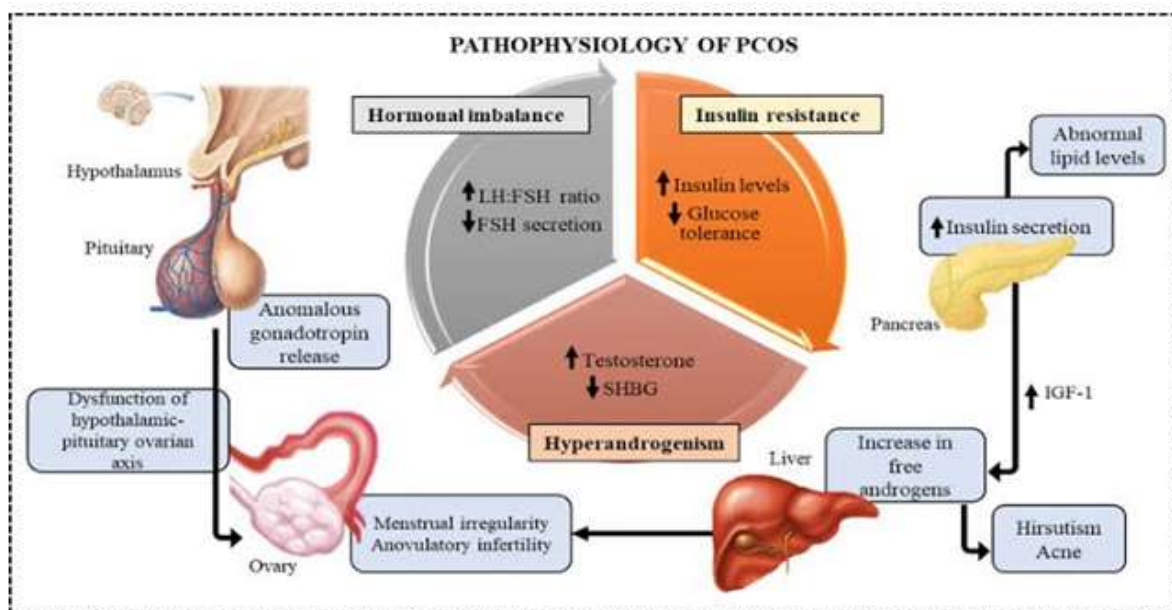
what is known insulin resistance which occur the body trouble to carry out normal action of insulin such as to regulate the blood – glucose levels. Insulin resistance cause by either genetic factor or lifestyle or combination of both.

What are Polycystic Ovaries? Polycystic Ovaries are the part of having PCOS. The menstrual cycle follicles develop and form Egg one of which is released during ovulation. The process is completed and the follicle are meant to break down and disappear. On an Ultrasound, the diagnosis of Polycystic Ovaries is confirmed. There are more than 10 follicles are visible on one ovary. This can result in acne increase in facial and body hairs and irregular periods.

**Pathophysiology**

Polycystic ovary syndrome is a chronic disorder with unknown etiology that was first described in 1935 by Stein and Leventhal. It is a reproductive, heterogeneous and metabolic disorder. Despite a large number of research studies, pathogenesis of PCOS still needs further elucidation. However, some pathophysiological mechanisms are known, e.g. alterations in the secretion of gonadotropin-releasing hormone,

defect in androgen synthesis and development of insulin resistance. A number of studies have a so indicated that insulin resistance is the key pathophysiological element for development of the syndrome. In addition to the characteristics that are inherent in PCOS, it is a common occurrence of metabolic and hormonal abnormalities associated with obesity, type 2 diabetes mellitus and dyslipidemia. The variety of metabolic disturbances in PCOS may be related to a higher risk of developing cardiovascular disease. Although PCOS has been traditionally considered a disorder that affects women in their reproductive years, clinical manifestations may be observed at menarche. According to research studies, the classical PCOS phenotype is linked to hyperandrogenism, anovulation and polycystic ovaries. The clinical manifestation of hyperandrogenism in these women varies in different ethnic groups, with external manifestations like oily skin, acne, hirsutism, central obesity, and even androgenetic alopecia. Factors such as dyslipidemia and obesity are all potent risk factors for cardiovascular disease, explaining why women with PCOS are more predisposed to hypertension.



**Symptoms**

Women experience other symptoms like-

- 1. **Psychological** : Anxiety , Depression, mental stress, mood swings etc.
- 2. **Reproductive:** Pregnancy complications, Infertility , Miscarriage etc.

- 3. **Menstrual** : Abnormal menstruation, heavy menstruation, irregular periods, short and light menstruation, absence of menstruation, oligo menorrhoea etc.

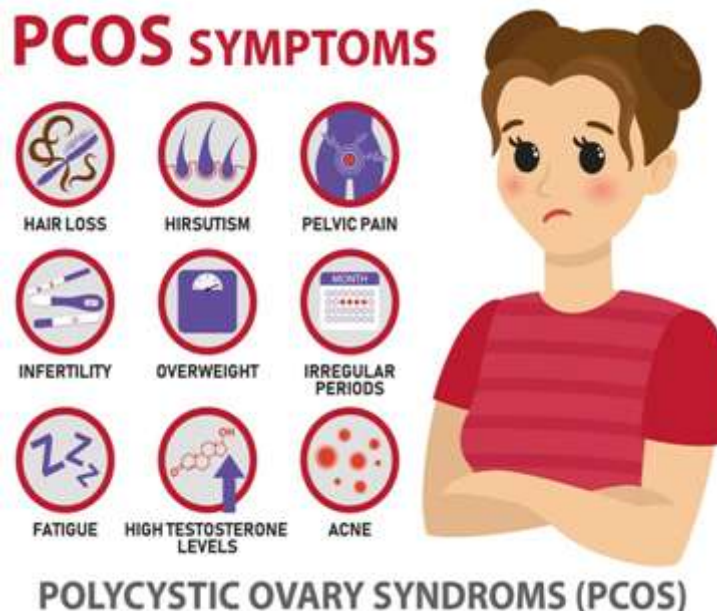
- 4. **Weight** : weight gain, obesity, or overweight

5. **Dermatological** : loss of scalp hairs, growth of unwanted hairs on skin, Hirsutism, dark patches on skin, inappropriate male features, etc.

6. **Metabolic**: Insulin resistance, type 2 diabetes, cardiovascular issues etc.

7. **Sleep** : Disordered sleep, sleep apnea etc.

The condition usually diagnosed by some factors like, Irregular menstruation, Failure to release an Egg from Ovary. Increase androgen hormone levels, excessive growth of facial hairs, raised levels of testosterone in blood.



**Diagnosis**

Diagnostic tools for PCOS -

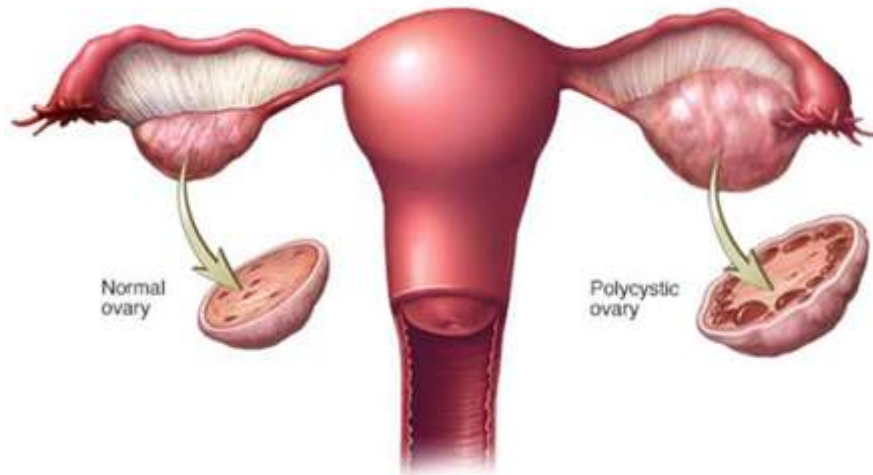
<b>Hyperthyroidism</b>	Over-production of thyroid hormones by thyroid gland. It can increase metabolism
<b>Hypothyroidism</b>	Inability of thyroid gland to produce enough thyroid hormones.
<b>Hyperprolactinemia</b>	Elevated prolactin levels in blood.
<b>Hyperandrogenism</b>	Excessive levels of male sex hormones in blood.
<b>Anovulation</b>	Egg is not released by ovary.
<b>Oligo ovulation</b>	Regular or infrequent periods.

There is no specific test for PCOS but doctor will consider the symptoms and will complete the physical examination.

- Physical examination:** Doctor will diagnose patient by asking him/her numerous questions about menstrual cycle of the patient. And examine the patient for physical sign of PCOS.  
E.g. Excessive growth of hair and dark skin.
- Blood test :** The blood of patient is examined for high cholesterol, blood sugar levels and

for change in levels of Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH).

- Transvaginal Ultrasound:** A long cylinder probe is inserted into the vagina to determine the presence of Ovarian Cysts or enlarged Ovaries and also to examine the reproductive organs. If you would prefer not to have a vaginal scan, doctor may conduct an ultrasound of your Abdomen. Done externally while the patient have full bladder.



**Treatment  
 Drugs for PCOS**

Some drugs are used to treat PCOS.

<b>Insulin resistant drug</b>	Metformin
<b>Hormonal therapy</b>	Oral contraceptive pills Clomiphene citrate Gonadotropins

**Insulin Resistant Drug:**

**1. Metformin –**

Metformin has been used for the past 15 years to reduce high level of insulin. It works to the body’s insulin response last longer so less insulin is produced. In addition, it may help to

reduce high male hormone level (androgens). Thus reducing hair growth, , it also improves menstrual irregularities and Ovulation. It can be used in combination with Clomiphene , a medication that stimulate ovulation.



**Mechanism of Action :**

- Decrease hepatic glucose production through a mild inhibition of the mitochondrial respiratory chain complex.
- Decrease intestinal absorption of glucose.
- Anti-oxidative properties of Metformin on endothelial cells.

**Effects :**

- Restoring ovulation
- Reducing the risk of miscarriage
- Reducing the risk of diabetes mellitus
- Reducing circulating androgen levels
- Reducing weight

**Side effects :**

- Mood changes
- Weight gain / loss

- Bloating and breast tenderness
- Glucose tolerance

**Administration / dose :**

- It is manufactured in Tablet dosage form.
- Dose ranging from 50 mg to 500 mg per day ,according to the patient.

**Hormonal therapy :**

**1. Oral contraceptive pills :**

It is also known as Birth Control Pill. It can help to regulate menstrual periods and to reduce menstrual cramps. It contains Estrogen and Progesterone which takeover the body's normal hormonal control of the menstrual cycle and Ovulation. It also helps to reduce the Testosterone levels. Which reduces the symptoms like Hairiness and acne.



**Mechanism of Action:**

- Estrogen Elevates the secretion of FSH via negative feedback on the Anterior Pituitary. And suppress the development of the Ovarian follicle.
- Progesterone inhibits the secretion of LH and prevents the Ovulation. It also makes the cervical mucus less suitable for the passage of sperm.
- Estrogen and progesterone act concert to alter the endometrial lining in such a way to discourage implantation. They may also interfere with the coordinated contractions of cervix uterus and the fallopian tube that facilitates the fertilization and implantation.

**Effects: :**

- To prevent pregnancy by inhibiting the Ovulation to also prevents sperm from penetrating cervix.
- Decrease the menstrual symptoms such as irregular periods, and intermenstrual bleeding.

- To restore the iron deficiency due to blood loss.
- To reduce premenstrual tension.

**Side effects:**

- Mood change
- Weight gain/ loss
- Fluid retention
- Mild nausea
- Flushing
- Dizziness
- Depression in pigmentation
- Skin changes
- Amenorrhea of variable duration while taking the pill.

**Administration / Dose :**

- It is manufactured in pill dosage form.
- Take 1 pill a day for 21 days. Skip 7 days. Then repeat the cycle.

**1. Clomiphene citrate : (Serophene )**

It is oral medication used for the treatment of Infertility. It is often given in case to induce

ovulation in women that do not develop and release an Egg on their own. Women who do not ovulate (without drugs) are said to have a condition called **Anovulation**. The most common cause of Anovulation is Polycystic ovarian syndrome.



**Mechanism of Action :**

- Clomiphene triggers the pituitary gland to secrete an increased amount of FSH and LH. This action stimulates the growth of ovarian follicle and this initiates ovulation.
- During a normal menstrual cycle, only one Egg is ovulated.

**Uses :**

- Used in the treatment of male hypogonadism as alternative to Testosterone replacement therapy
- Used to induce ovulation in women who do not produce Egg.
- Used to treat infertility in women.

**Side effects:**

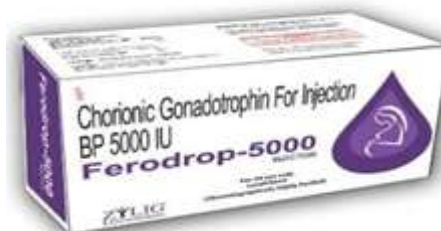
- Mood swings
- Physiological – emotional side effects
- Hot flushes
- Abdominal discomfort
- Visual disturbances
- Nausea
- Ovarian Cysts formation
- Thinning of the uterine endometrial lining
- Reduce the production of cervical mucus, this can lower fertility.

**Administration/ dose :**

- Clomiphene is manufactured in tablet dosage form and is taken orally.
- Usually taken once a day for consecutive 5 days.

**2. Gonadotropins:**

Also known as GnRH , LH-RH . They are hormones made by hypothalamus. GnRH cause pituitary gland in the brain to make and secrete the LH and FSH. In men, these hormones cause the testicles to make testosterone. In women, they cause ovaries to make Estrogen and progesterone.



**Mechanism of Action :**

- Gonadotropin receptors are embedded on the surface of target cells and coupled to G-protein system
- Gonadotropins are released under the stimulation of Gonadotropins releasing Hormone. (GnRH)
- Gonads (testes and ovaries) are the primary Target organs for LH and FSH.
- The gonadotropins affects multiple Target cells.

**Uses :**

- Used in during fertility treatment such as Intrauterine insemination. In- vitro fertilization
- Injection of gonadotropins are started in early menstrual cycle to cause multiple eggs to grow to a mature size .

**Side effects:**

- Bloating
- Headache
- Breast tenderness
- Upset stomach
- Hot flashes
- Mood swings

**Administration :**

- It is available in the form of IM injections.

**Preventive measures**

- 1. Diet :** The diet has been an important factor for PCOS . Fats and proteins from one's diet can form advanced glycation end product when exposed to sugar in blood stream .  
E.G. grains, legumes, nuts, seeds, fruits, fish, leafy greens, fatty salmon etc.
- 2. Exercise :** To achieve the best results exercise should include aerobics, weight / resistance training, combination of both exercises .

**3. Lifestyle:** Everyday habits greatly affects the development and severity of PCOS. Obesity is the reason of PCOS. Exercise helps to reduce PCOS symptoms like depression, inflammation and excess weight. Increase daily activities by taking the stairs going on short walk and stretching through out the day.

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