

# POLYCYSTIC OVARIAN SYNDROME - A REVIEW

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**Abstract:** Polycystic ovary syndrome (PCOS) is a problem in which a woman's hormones are out of balance. Most women with PCOS grow many small cysts on their ovaries. That is why it is called polycystic ovary syndrome. The cysts are not harmful but lead to hormone imbalances. PCOS seems to run in families, so chance of having it is higher if other women in the family have it or have irregular periods or diabetes. Polycystic ovarian disease (PCOD) is caused due to the increased level of sex hormones in females and it may also occur due to the presence of ovarian cysts. In PCOD the enlargement of ovary occurs. Some symptoms of PCOD are irregular menstruation, obesity, excessive hair growth, etc. The prolonged PCOD leads to diabetes, heart disease and endometrial cancer. There is no any particular diagnostic test or treatment for PCOD. Classic symptoms include amenorrhea, hirsutism, acne, and obesity, irregular periods. Management of PCOS is directed by the client's concerns regarding symptoms, desire for pregnancy, and degree of morbidity related to androgen excess. The management of PCOS includes diet modification, weight loss, and stress management, hormonal therapy, monthly or bimonthly administration of medroxyprogesteron. To know more about the symptoms, diagnosis and management of Polycystic ovarian syndrome.

**Keywords:** Hormone level, diabetes, acne, hirsutism

## Introduction

Polycystic Ovarian Disease(PCOD) is one of the endocrine condition which is most commonly seen in women of pubertal age, with prevalence rates of range between 7-11%. It has varying of incidence from 6% to 10%. Polycystic ovarian syndrome is seen in child growing age of women group across all cultures, and ethnicities. A study shows that Indian adolescents reported of polycystic ovarian syndrome has incidence of 9.13%. The common clinical features of PCOD are hyperandrogenism like seborrhoea, hirsutism, frank virilization, acne, alopecia and irregular and anovulatory cycles with polycystic ovaries on pelvic sonography. Polycystic ovary syndrome is a common heterogeneous condition. The phenotype varies widely depending on, lifestyle and bodyweight including genotype, ethnicity and environmental factors[1].

In Recent times PCOD has been commonly associated with obesity insulin-resistance (IR), and a risk of developing Type 2 diabetes mellitus (T2DM). Polycystic ovary syndrome (PCOS) is of public health importance as it is very common, because it affecting up to one in five women of reproductive age. It has significant and diverse clinical implications including reproductive metabolic obesity, type 2 diabetes mellitus, adverse cardiovascular risk profiles and psychological features increased anxiety, depression and worsened quality of life. It may be considered as a cosmetic issue because of hirsutism and acne, or as a gynaecological Problem that leads to irregular menstruation and reduced fertility. Proper early diagnosis and treatment for PCOD is important[2]. Prolonged medications and lifestyle changes are essential for a successful outcome. Common type of the investigations usually done for Polycystic ovarian disease are hysteroscopy, Laparoscopy, hormonal investigations, ultrasound scan. In these investigations Ultrasound scan are commonly used. The treatment of infertility for overweight women should always include weight loss, exercise, food control and skin care. The clinician should inquire about, and examine for, the presence any male-pattern that is hair located on the upper lip, chest, chin inner aspects of the thighs and lower abdomen. Signs of androgenism shows oily skin and acne but hirsutism

is the most common manifestation of the androgen component of polycystic ovarian syndrome. During the past decade, chronic anovulation and hyperandrogenism shows commonly in women to have an increased risk of increased risk factors for coronary heart disease (CHD) and diabetes. Management of polycystic ovarian syndrome should be based on education, addressing psychological factors, support and strongly emphasising healthy lifestyle with targeted medical therapy as required[3].

#### Symptoms

Hyperandrogenism (acne, hirsutism, alopecia – not virilisation)

Menstrual disturbance

Infertility

Obesity

Sometimes asymptomatic, with polycystic ovaries visible on ultrasound scan

Serum endocrinology

Fasting insulin (not routinely measured; insulin resistance or impaired glucose tolerance assessed by glucose tolerance test)

Androgens (testosterone and androstenedione)

Luteinising hormone, usually normal follicle stimulating hormone

Sex hormone-binding globulin, results in elevated 'free androgen index' oestradiol, oestrone (neither measured routinely as wide range of values)

Prolactin

Possible late sequelae

Diabetes mellitus

Dyslipidaemia

Hypertension and cardiovascular disease

Endometrial carcinoma

Breast cancer

#### Etiology

PCOS can be described as an oligogenic disorder in which the interaction of a number of genetic and environmental factors determine the heterogeneous, clinical, and biochemical phenotype. Although the genetic etiology of PCOS remains unknown, a family history of PCOS is relatively common; however, familial links to PCOS are unclear[4]. A lack of phenotypic information prevents a formal segregation analysis. Nonetheless, the current literature suggests that the clustering of PCOS in families resembles an autosomal dominant pattern.

Environmental factors implicated in PCOS (e.g., obesity) can be exacerbated by poor dietary choices and physical inactivity; infectious agents and toxins may also play a role. The reproductive and metabolic features of PCOS are sometimes reversible with lifestyle modifications such as weight loss and exercise[5].

#### Genetics of PCOD

PCOS has long been noted to have a familial component. Genetic analysis has been hampered by the lack of a universal definition for PCOS. Most of the criteria used for diagnosing PCOS are continuous traits, such as degree of hirsutism, level of circulating androgens, extent of menstrual irregularity and ovarian volume and morphology. To perform genetic analyses, these continuous variables have to be transformed into nominal variables[6]. Family studies have revealed that about 50% of first-degree relatives have PCOS, suggesting a dominant mode of inheritance. Commonly first-degree male relatives appear more likely to have premature baldness. As hyperandrogenism is a key feature of PCOS it is logical to explore the critical steps in steroidogenesis and potential enzyme dysfunction. A number of studies have found an abnormality with the cholesterol side chain cleavage gene (CYP11a), although this is debated[7].

It has been hypothesised that polymorphisms in the INSR gene that induce mild changes in insulin receptor function may contribute to the development of PCOS, as it is unlikely that a major mutation is present given the wide variability of insulin resistance in women with PCOS. The insulin gene variable number of tandem repeats (VNTR) minisatellite locus which lies to the insulin gene on chromosome and regulates the expression of the insulin gene. The class III allele of the insulin VNTR gene is associated with anovulatory PCOS[8].

While it is beyond the scope of this review to provide a more detailed account of the various genetic studies that have been performed to date, there is substantial evidence for genetic defects in steroidogenesis and insulin action being involved in the pathogenesis of PCOS. The pathophysiology of PCOS therefore involves a combination of genetic abnormalities combined with environmental factors, such as nutrition and body weight, which affect expression of the syndrome[9].

#### Diagnosis of PCOD

##### History-taking

Specifically for menstrual pattern, obesity, hirsutism and the absence of breast development. If obese, the time of onset, progression and problems should be explored. Diet, exercise and smoking need evaluation are lifestyle parameters and age of onset and progression of hirsutism and/or acne. Some of the medications used and effects of medication on acne and hirsutism should also be included. Menstrual disorders, infertility, hirsutism and age of puberty and in female relatives should be included in the family history[10].

### Physical examination

Obesity, body mass index blood pressure, presence of acne, general body habits and evidence of acanthosis are observed in physical examinations. The distribution and severity of hirsutism should be observed clinically and evaluated. Polycystic ovarian syndrome in females will generally associated with hyperandrogenism such as masculine body, clitoromegaly, deepening of voice should alert one to the possibility of virilizing adrenal/ovarian tumours or congenital adrenal hyperplasia[11].

### Gynecologic ultrasonography

It looks for small ovarian follicles. According to the Rotterdam criteria, or more small follicles should be seen in an ovary on ultrasound examination. The numerous follicles contribute to the increased size of the ovaries that is 1.5 to 3 times larger than normal[12]?

### Laboratory tests

1. Serum levels of androgens, including androstenedione and testosterone may be elevated. Dehydroepiandrosterone sulfate (DHEA-S) levels above 700-800 mcg/dL are highly suggestive of adrenal dysfunction. The free testosterone level is thought to be the best measure, with about 60% of PCOS patients demonstrating high levels.
  2. The ratio of LH (Luteinizing hormone) to FSH (Follicle stimulating hormone) is greater than 1:1 (sometimes more than 3:1), as tested on day 3 of the menstrual cycle.
  3. Fasting biochemical screen and lipid profile.
- Two-hours oral glucose tolerance test (GTT) in patients with risk factors (Obesity, family history, history of gestational diabetes) may indicate impaired glucose tolerance (insulin resistance) in patients with PCOS.
4. Fasting insulin level or GTT with insulin levels (also called IGTT): Elevated insulin levels have been helpful to predict response to medication and may indicate patients who will need higher doses of metformin or the use of a second medication to lower insulin levels. A hypoglycemic response in which the two-hour insulin level is higher and the blood sugar lower than fasting is consistent with insulin resistance. A mathematical derivation known as the HOMAI, calculated from the fasting values in glucose and insulin concentrations, allows a direct and moderately accurate measure of insulin sensitivity (glucose-level x insulin-level/22.5[15-17].

### MANAGEMENT OF METABOLIC DISTURBANCES

Insulin resistance (and compensatory hyperinsulinemia) is an important factor in maintaining hyperandrogenemia by acting directly on theca cells inducing excess androgen production. Insulin also acts as a co-gonadotropin, increasing the effect of LH on ovarian androgen secretion. Metformin, a biguanide, has been widely used for PCOS patients, and evidence indicates it is beneficial for women with PCOS with metabolic syndrome and/or obesity, as well as for affected women who have impaired glucose tolerance, since the efficacy of metformin for diabetes prevention has been demonstrated in individuals with pre-diabetes[18]. Its main action is in the liver, with suppression of gluconeogenesis and hepatic glucose output, but it also enhances peripheral insulin action, and reduces glucose absorption from the digestive tract, with no significant direct effect on pancreatic insulin production. Metformin also directly inhibits thecal androgen production. In women with PCOS, treatment with metformin has been shown to ameliorate the cardiometabolic profile by improving insulin sensitivity, lowering blood glucose and androgen levels and possibly by its effects on body weight. These effects of metformin are more potent when it is combined with lifestyle intervention. Diets with low caloric intake are part of the treatment and those with low glycemic index appear to be better adjusted for PCOS patients[19].

It is important to underscore, however, that the first-line treatment for hirsutism, menstrual irregularities and infertility are antiandrogens, contraceptive steroids, and clomiphene citrate, respectively. While metformin is more effective than oral contraceptives in reducing fasting insulin and not increasing triglycerides, it is less effective in improving menstrual pattern, hirsutism or decreasing testosterone. Importantly, there is no evidence of benefits in the absence of insulin resistance[20].

Metformin is also a reasonable treatment option for those women to whom oral contraceptives may not be recommended, such as PCOS patients presenting moderate to severe high blood pressure, high triglycerides levels, class II or III obesity and/or metabolic syndrome. In this case, and especially if antiandrogen drugs are added to the treatment, other options for contraception should be recommended, including progestogen only pills (mini-pill) or IUDs.

The usual dose of metformin for PCOS is 1,500 to 2,500 mg per day. A main limitation can be side effects, which are predominantly gastroenterological, consisting of abdominal discomfort, nausea, and diarrhea. These symptoms are usually dose-dependent and can be minimized by gradually increasing the dose of metformin over a period of 1-2 months. Initial doses should be 250-500 mg/day, taken just before the main meal. In the case gastrointestinal side effects recidivate, the current dose may be reduced for a period of 7-10 days, followed by a resumption of the dosage increase. Hepatic and renal function should be monitored before and during treatment. Specific additional treatment for high blood pressure, dyslipidemia or obesity may be needed for individual PCOS women. Additionally, bariatric surgery may be another option for severe obesity or obesity with metabolic comorbidities reducing insulin resistance[21-23].

### Non pharmacological

Weight reduction for obese patients with PCOS is beneficial in many ways. Weight loss helps to decrease androgen, luteinizing hormone (LH), and insulin levels. It also helps to regulate ovulation, thereby improving the potential for pregnancy. Laparoscopic ovarian drilling is an outpatient surgical intervention in which multiple perforations are created in the ovarian surface and stroma. It is thought that this intervention destroys androgen-producing tissue, which should lead to decreased androgen levels. It has been found to be as effective as medical interventions without increasing the risk of multiple pregnancies. reducing insulin resistance[24].

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#### PCOS IN MENOPAUSAL TRANSITION AND POST- MENOPAUSE: ARE THERE SPECIFIC FEATURES

In menopausal transition, there may be an amelioration of clinical features. In fact, there is a trend towards more regular cycles and improvement on hirsutism with aging. This is in part due to the well-known decrease in androgen secretion from the third to the fifth decade of life that occurs in normal women and has been also reported in PCOS. In addition, ovarian volume decreases along with pre- menopause and menopause transition, as previously reported. Thus, alterations in ovarian volume and morphology may be less evident in PCOS during menopausal transition, and PCO criteria are not useful after menopause.

In fact, no specific clinical presentation during menopause has been established, and the diagnosis of PCOS is, in general, confirmed before this period, based on the history of oligomenorrhea and hyperandrogenism. Additionally, clinical or biochemical hyperandrogenism appearing in previously normal peri- or post-menopausal women should be carefully investigated in order to screen them for androgen-secreting tumors [25-26].

#### Endometrial cancer

Endometrial adenocarcinoma is the second most common female genital malignancy but only 4% of cases occur in women less than 40 years of age. The risk of developing endometrial cancer has been shown to be adversely influenced by a number of factors including obesity, long-term use of unopposed oestrogens, nulliparity and infertility. Women with endometrial carcinoma have had fewer births compared with controls and it has also been demonstrated that infertility per se gives a relative risk of two. Hypertension and type 2 diabetes mellitus have long been linked to endometrial cancer, conditions that are now known also to be associated with PCOS. The true risk of endometrial carcinoma in women with clearly defined PCOS is, however, difficult to ascertain.

Endometrial hyperplasia may be a precursor to adenocarcinoma, although the rate of progression is difficult to predict. While the degree of risk has not been clearly defined, it is generally accepted that for women with PCOS who experience amenorrhoea or oligomenorrhoea, the induction of artificial withdrawal bleeds to prevent endometrial hyperplasia is prudent management. Indeed it is considered important that women with PCOS shed their endometrium at least every three months. For those with oligo- or amenorrhoea who do not wish to use cyclical hormone therapy an ultrasound scan to measure endometrial thickness and morphology is recommended every 6–12 months (depending upon menstrual history). An endometrial thickness greater than 10mm in a woman with amenorrhoea warrants an artificially induced bleed, which should be followed by a repeat ultrasound scan and endometrial biopsy if the endometrium has not been shed. Another option is to consider a progestogen-secreting intrauterine system.

#### Breast cancer

Obesity, hyperandrogenism and infertility occur frequently in PCOS and are features known to be associated with the development of breast cancer. However, studies examining the relationship between PCOS and breast carcinoma have not always identified a significantly increased risk. The study by studies shows that relative risk of 1.5 (95% CI 0.75–2.55) for breast cancer in the group of women with chronic anovulation, which was not statistically significant. After stratification by age, however, the relative risk was found to be 3.6 (95% CI 1.2–8.3) in the postmenopausal age group. Pierpoint et al. [13] assessed mortality from the national registry of deaths and standardised mortality rates calculated for women with PCOS compared with the normal population. The average follow-up period was 30 years. The standardised mortality rate for all neoplasia was 0.91 (95% CI 0.60–1.32) and for breast cancer 1.48 (95% CI 0.79–2.54). Breast cancer was the leading cause of death in this cohort.

#### Ovarian cancer

In recent years there has been much debate about the risk of ovarian cancer in women with infertility, particularly in relation to the use of drugs to induce superovulation for assisted conception procedures. The risk of ovarian cancer appears to be inherently increased in women who have multiple ovulations that is those who are nulliparous (possibly because of infertility) with an early menarche and late menopause. Thus, it may be that inducing multiple ovulations in women with infertility will increase their risk – a notion that is by no means proven. Women with PCOS who are oligo- or anovulatory might therefore be expected to be at low risk of developing ovarian cancer if it is the lifetime number of ovulations rather than pregnancies that is critical. Ovulation induction to correct anovulatory infertility aims to induce unifollicular ovulation and so, in theory, should raise the risk of a woman with PCOS to that of a normal ovulating woman. The polycystic ovary, however, is notoriously sensitive to stimulation and it is only with the development of high-resolution transvaginal ultrasonography that the rate of unifollicular ovulation has attained acceptable levels. There are a few studies which have addressed the possibility of an association between polycystic ovaries and ovarian cancer. The results are conflicting and the ability to generalise is limited owing to problems with the study designs [27].

#### Alternative medicine

Acupuncture is one of the alternative medicine modalities that had been emerging as one of the commonly used methods for treatment of PCOS. Acupuncture may help PCOS patients to regulate and manage their periods. Moreover, it may help in decreasing body weight, reducing headache and improving patients' mood. Acupuncture needles are placed in the areas where it is near to the reproductive system and it also placed near to the area where the blood vessels are involved to the reproductive system. regulating the level of hormone help in proper maintaining and functioning of the reproductive system.

There is insufficient effect from D-chiro- inositol polycystic ovarian syndrome .But , myo-inositol shows effective activity .It is capable of restoring spontaneous ovarian activity and fertility in PCOS patients[28].

### Prognosis of PCOS

Endometrial hyperplasia and endometrial cancer, insulin resistance and type II diabetes, hypertension, depression, psychological disorders, dyslipidemia, cardiovascular diseases, cerebrovascular stroke, weight gain, sleep apnea, non-alcoholic fatty liver disease, acanthosis nigricans (patches of darkened skin under the arms, in the groin, on the back of the neck) and autoimmune thyroiditis are risk of polycystic ovarian syndrome in women. Early diagnosis and treatment may reduce the risk of these complications, such as type 2 diabetes and heart disease.

### Conclusion

There are still lacking knowledge about many of its aspects, including its etiology, progression throughout life, spectrum of symptoms, and various morbidities. The pathogenesis of PCOS remains obscure, with unregulated steroidogenesis, insulin resistance, oxidative stress, and genetic factors contributing, possibly from prenatal life, to the disease. Supplementary studies are needed to bridge between the various susceptibility factors that might contribute to PCOS.

The current diagnostic guidelines are still vague and might not detect patients with less severe non-classic phenotypes. The guidelines in adolescents lack specificity, as they might fail to differentiate between normal development and pathogenesis. Since proper diagnosis is a crucial step to initiate treatment and prevent future morbidities, further clinical research should seek not only to update and unify guidelines but also to provide an appropriate rationale for diagnostic tools that can detect all PCOS phenotypes[29].

Morbidities, more common in the frank PCOS phenotype, emphasize the complexity of this disease as a condition that affects many bodily systems, whether endocrine, gynecological, cardiac, or psychological. Therefore, the management of this varied entity requires a skilled and knowledgeable multidisciplinary team who can achieve best patient outcomes. It is imperative to remember that the treatment of PCOS changes throughout age and should be guided by symptomatology. Early detection of long-term morbidities through appropriate screening tests constitutes an essential part of the management of this condition. Guidelines strongly recommend lifestyle modifications as a critical part of the management and some medical management are advised for early treatment of polycystic ovarian syndrome.

Polycystic ovary syndrome is one of the complex disorder in number of treatment are needed. Clomiphene has shown one of the best outcome in treating infertility, but in which results are limited regarding the pharmacological treatment of androgenic symptoms. Long-term consequences of PCOS, which include type-2 diabetes and cardiovascular disease, can be treated with antidiabetic drugs and statins[30].

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