

## PREVALENCE AND RISK FACTOR OF POLYCYSTIC OVARIAN SYNDROME

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## ABSTRACT

Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder in women. Its clinical manifestation varies from mild to severe disturbance of reproductive and metabolic functions. PCOS is clinical and public health importance because it is affecting up to one in five women of reproductive age. It is an X-linked dominant condition and has diverse clinical implications such as psychological features (anxiety, depression), reproductive features (hirsutism and hyperandrogenism), and impaired glucose tolerance. It is widely dependent on environmental, genetic, ethnicity factors including lifestyle and body weight. Weight loss improves the endocrine profile and increases chances of ovulation and pregnancy. It can be treated with medications such as clomiphene citrate, tamoxifen, aromatase inhibitors, and gonadotrophins. The last option for fertilization is *in vitro* fertilization when other treatment fails. Its prevalence is estimated at 4-8% from studies performed in Spain and USA. Lifestyle including diet, exercise, and behavior therapy improves fertility. PCOS has unique interactions with the ever increasing obesity prevalence worldwide as obesity-induced insulin resistance significantly aggravates all the features of PCOS. Education about how PCOS affects long-term health should be provided to women with this disorder to feel physical and psychological benefits so that they could engage themselves more with their health care providers.

**Keywords:** Polycystic ovarian syndrome, Hyperinsulinemia, Hormone disbalance, Hirsutism, Ovarian cyst, Obesity, Sleep disorders.

## INTRODUCTION

Polycystic ovarian syndrome (PCOS), Stein-Leventhal syndrome, or hyperandrogen anovulation syndrome are a common hormonal condition which was first diagnosed by physicians in 1930. It is called a syndrome because it refers to a number of symptoms which are experienced at the same time. It is both emotionally and physically challenging. In the 20<sup>th</sup> century, polycystic ovarian disease condition was poorly understood. On 3 December, 2012, National Institutes of Health held a conference on this disorder and sponsored an evidence-based methodology workshop which clarifies its benefits, drawbacks, causes, predictors, long-term consequences and treatment and prevention strategies. Hormones are chemical messengers that trigger many processes including growth, development, and energy production; their job is to signal the release of other hormones. During each menstrual cycle, follicles develop and form eggs, one of which is released during ovulation. After this process, the follicles break down and disappear. With PCOS, these follicles stop growing and become cyst. Polycystic ovarian disease (PCOD) is a health issue in which female sex hormones gets disturbed, 12 or more tiny cysts in ovaries make a tiny amount of androgen (male sex hormone) that causes irregular periods. PCOS causes unwanted changes in the appearance of women and overtime, can lead to serious health problems such as heart diseases, diabetes, high cholesterol, and high blood pressure. PCOS is affecting 1 out of 15 females in the teen year and 25-30% in young women. It affects approximately 5 million women in the United States and also affects 11-year-old girls during puberty. In young girls, it causes acne, weight gain, facial hairs, male pattern baldness (alopecia) and affects their self-esteem, while in women it manifests an inability to conceive (infertility) [1-5].

In PCOS, ovulation does not occur properly in the young women due to which egg does not come out each month, progesterone is not made and the chances of pregnancy become low. Insulin resistance may occur, so doctors often prescribe the drugs which are used in the diabetic patients such as metformin, which improve insulin insensitivity. Hyperinsulinemia is one of the root causes behind PCOS. Treatment can

control the long-term problems and can cause the patient to ovulate. Other organs which are affected by PCOS are liver, heart, muscles, blood vasculature, and pancreas [6-10].

## SYMPTOMS

The symptoms of PCOS usually become apparent in teens and early 20s. It varies from women to women. Symptoms can vary from mild to severe conditions. The common symptoms of PCOS include unpredictable or irregular periods, many small cysts in the ovaries, high level of androgen and prolactin hormones, acne (occur after adolescence and does not respond to usual treatment), rapid weight gain, difficulty in losing weight, hirsutism (excess hair growth on face, chest, abdomen, upper thighs, back or buttocks, affect 70% of women with PCOS), mental health problems, metabolic dysfunction, difficulty getting pregnant, thinning hair and hair loss from the head, oily skin, depression and mood changes, patches of thickened velvety, darkened skin on the neck, arms, breast or thighs which is known as *Acanthosis nigricans*, pelvic pain and sleep apnea (breathing stops for short period of time), obesity (80% of women with PCOS are obese), fatigue (very low energy level all the time) [11-15].

## CAUSES

The exact cause of PCOS is not unknown but thought to be related with abnormal hormonal balance. In PCOS, women make more androgen than normal. High level of androgen affects the development and release of egg during ovulation. Hyperinsulinemia is also linked with PCOS. Insulin is a hormone, produced by the pancreas that regulates and controls the change of sugar, starches, and other food into energy. It moves the sugar from blood into cells; where sugar is broken down to liberate energy. Insulin resistance means the body cells are resistant to insulin. The body, therefore, has to make extra insulin to compensate. High insulin produces too much of testosterone hormone which further affects ovulation. Excess insulin produces androgen, which further causes acne, hirsutism and problem in ovulating. Insulin resistance makes PCOS symptoms worse by inducing weight gain in females, which lead to excess fat. Others hormones, such as luteinizing hormones (LH) (which stimulates ovulation), prolactin (hormone that stimulates

breast glands to produce milk), and sex hormone binding globulin, are also raised in PCOS. Raised levels of LH have abnormal effects on ovaries. Low levels of Sex hormone binding globulin decrease the high level of testosterone. PCOS runs in progeny sometimes, if mother, sister or aunt, have PCOS then its risk is often increased. Genes which are linked in this disorder are not identified yet. Recently, Genome Wide Association Studies have identified some genes that merit further studies. Every individual experiences this syndrome in the context of her own reproductive health and quality of life concern [16-20] (Fig. 1).

## DIAGNOSIS

Doctor takes medical history (menstrual periods, weight changes, etc.) and physical exam (blood pressure, body mass index [BMI], and waist size) [21-24]. He will also check areas of increased hair growth. He might check ovaries, if they are enlarged or swollen by the increased number of small cysts. Blood test is done to check cortisol, insulin, thyroid hormone, androgen, dehydroepiandrosterone sulfate, glucose levels, LH and follicle stimulating hormone, examination of the endometrium (lining of the womb). This lining becomes thick, which is known as endometrial hyperplasia, if periods are not regular. This condition increases the risk of endometrial cancer. Serious health problems associated with PCOS are risk of heart attacks, high blood pressure (4-7 times more than normal female), metabolic syndrome, diabetes or pre-diabetes in 50% of women before 40 years of age. High level of low-density lipids cholesterol and low level of high-density lipids [25-30].

## TREATMENT

Until now, PCOS is considered as incurable disorder, it is managed to prevent problems. Treatment is tailored according to symptoms, health problems or whether she wants to get pregnant or not. Some treatments are lifestyle modifications such as physical exercise (30 minutes, at least, 3 times a week) to reduce weight and obesity, even a weight loss of 10-15 pounds is useful in regulating proper menstrual cycle, eating healthy food, maintain BMI (between 19 and 25). Healthy tips include limited processed food and food with added sugars. The addition of whole grain products, lean meats, fruits in diet, helps to lower blood glucose level, improves insulin level and normalizes raised hormonal level in the body. Healthy fats and protein over butter, mayonnaise, red meat, etc. can be given. Sugar-free drinks like water, diet soda and flavored water should be given instead of sugary drinks. Around 10% loss in bodyweight helps in normal period and makes the menstrual cycle more regular. Birth control pills (which are the combination of estrogen and progestin) help to clear acne and control menstrual cycle. Pills which have progesterone alone, do not help in reducing acne and hair growth, it can only prevent endometrial cancer. Their mechanism includes inhibition of peripheral conversion of testosterone

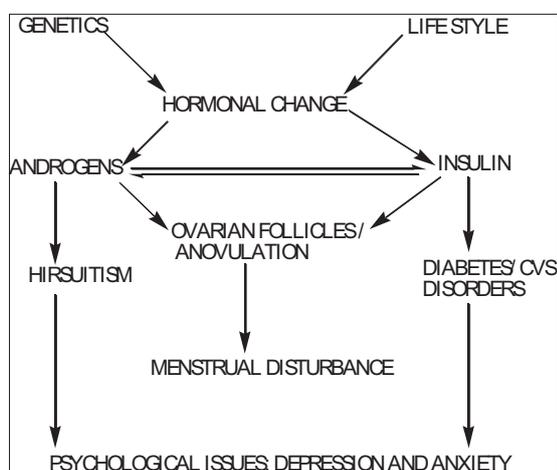


Fig. 1: Causes of polycystic ovarian syndrome

to dihydrotestosterone and binding of dihydrotestosterone to androgen receptors. Diabetes medications also help in reducing PCOS symptoms, although this medication is not approved by US Food and Drug Administration [31-34]. Metformin, thiazolidinediones slows down the growth of abnormal hair, decreased body mass, improved cholesterol level, androgen secretion and helps ovulation. Fertility medications help women to become pregnant, although some fertility medications have also increased the chances of twins and triplets.

Treatment options are clomiphene (first choice therapy to stimulate ovulation), Metformin with clomiphene help in ovulation in a small dose. Gonadotrophins, given as shots but have a risk of multiple births. Other basic fertility treatments are intrauterine insemination, endometrial biopsy, cyst aspiration, laminaria insertion, cervical dilation, hysterosonogram, follicle puncture. Ovarian drilling or follicle puncture increases the chances of ovulation and is used sometimes when the patient does not respond to fertility medicines. A cut is made above and below navel, small tool that acts like a microscope is inserted in the abdomen, which punctures the ovary with a small needle carrying an electric current. This surgery carries a risk of developing scar tissues on ovary, and does not help with loss of scalp hairs and increased growth of hair growth. Other advanced fertility treatments are *in vitro* fertilization, Gamete intrafallopian transfer. These treatments are very costly, offers the best chance of becoming pregnant and it has control over multiple birth defects. Medicines called anti-androgen reduces hirsutism and clean acne for example spironolactone. Occasionally, spironolactone causes fatigue, postural hypotension and dizziness and when administered alone at a high dose, it causes menstrual irregularity. Finasteride, a medicine used by men for hair loss, has a same effect. These drugs are often combined with birth control pills. Pregnant and breastfeeding women should avoid this medication. Other treatments are eflornithine hydrochloride to reduce facial hair, laser hair removal or electrolysis. Laser hair removal damage hair follicles but is harmful too as it has a potential for depigmentation and scarring in darker skinned women [35-38]. Bariatric (weight loss) surgery is also very effective in PCOS. Drugs like troglitazone showed improved results in this disorder, but now it is taken off in the market because it causes liver problem. Glucocorticoids 5-7.5 mg, Prednisolone once or twice daily have shown to improve hirsutism in women and congenital adrenal hyperplasia [39-42]. Overdosing can lead to weight gain, decreased bone mineral density. Gonadotropin-releasing hormone agonist is effective and expensing method in severe insulin resistance. It suppresses pituitary hormones and decreases androgen secretion. Medications alone have not shown any good effect in PCOS [43-45].

## PCOD, AFFECTING PREGNANT WOMEN

Pregnant women have higher rates of miscarriage, gestational diabetes, premature delivery, pregnancy-induced high blood pressure (preeclampsia) with PCOS. Babies have a higher risk of spending time in neonatal intensive care unit during or after birth. Metformin lowers androgen level in pregnant women and does not cause birth defects. It should not be used during breast feeding because it passes through milk [46-50].

## CONCLUSION

PCOS is a chronic disease and represents a major health and economic burden. No one is quite sure what causes this syndrome. It is a result of both genetic and environmental factors. PCOS refers to the enlarged ovaries that contain tiny cysts. Women dealing with the challenges of PCOS should banish negative self-talk, self-critical thoughts and should start treating themselves with a worthwhile person to improve their self-esteem. Stop taking too much of stress, which could be a main cause of PCOS. Overall further researches are necessary for this complex condition. Scientist is trying to better understand this disorder, which is defined an excess production of male hormones, irregular ovulation, and cyst.

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