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An Overview: Polycystic Ovary Syndrome and Related Future Methods

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Abstract
Polycystic ovary syndrome (PCOS) is a common hormonal disorder that affects females with ovaries, typically during their reproductive years. Many signs are present, such as irregular menstrual periods, elevated levels of androgen (male hormone), and the development of cysts—small, fluid-filled sacs—on the ovaries. Its symptoms progress from minor to severe, such as the first signs of hirsutism and acne, which worsen and cause irregular menstruation and infertility. Insulin resistance, weight gain, infertility, and a higher risk of type 2 diabetes and cardiovascular disease are just a few of the health issues that PCOS can cause. While the precise etiology of PCOS remains unclear, a hereditary and environmental combination is thought to be involved. Numerous diagnostic instruments are available, including blood testing for insulin resistance and ultrasonography. Depending on the patient's needs, therapy options for PCOS may include Ayurveda medicine, hormone medication, lifestyle modifications, and fertility therapies. PCOS treatment options typically center on treating symptoms. The long-term health risks associated with PCOS must be reduced by early diagnosis and appropriate management. There are various forms of future perception, including Determining the factors that contribute to the onset and progression of PCOS after birth and clarifying the underlying mechanisms, clarifying the processes that underlie PCOS's high heredity, finding biomarkers that might be utilized to identify those who are highly likely to have PCOS in their early years.

Keywords: PCOS Insulin resistance, Ayurvedic management, Future treatment.

1. Introduction

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder that impacts many women of reproductive age worldwide. This syndrome is frequently linked to enlarged and dysfunctional ovaries, high levels of androgen, insulin resistance, etc [1]. One in ten women may have been struggling with PCOS and its problems before menopause [2].

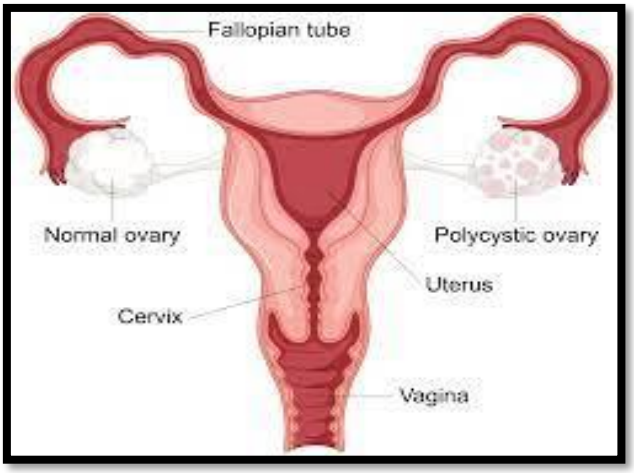
It is characterized by an extremely irregular menstrual cycle in which ovulation does not occur. The major endocrine glands involved in PCOS are the hypothalamus, pituitary gland, ovaries adrenal gland, and peripheral adipose tissue which together contribute to create a general imbalance [3]. The primary causes of PCOS are known to be a high luteinizing hormone (LH) to follicle-stimulating hormone (FSH) ratio and an increased frequency of gonadotropin-releasing hormone (GnRH) [4]. The role of several internal and external factors, including insulin resistance (IR), hyperandrogenism (HA), environmental factors, genetics, and epigenetics, is suggested by the evidence [1]. A PCOS patient's ovaries contain more than

ten follicles visible on ultrasound. The polycystic ovary, in comparison to the normal ovary, its layer has more follicles and a dense center. This center is known as the stroma which is where testosterone is made Selective insulin resistance is central to the etiology of PCOS [5].

In addition, it is worth mentioning that PCOS increases the risk of further complications like cardiovascular diseases, type 2 diabetes mellitus, metabolic syndrome, depression, and anxiety[1]. Every woman with PCOS is advised to follow a regular exercise schedule and a diet low in fat and sugar to treat this illness, as losing at least 5% of body weight is the most important first step and different types of oral contraceptives, antiandrogen agents, insulin sensitizers, and ovulation inducers are used.

Given that PCOS is a growing issue that is unfortunately followed by many unwanted complications and that available methods and medications are not 100% effective, it is essential to investigate its pathogenesis and find new pharmacological targets carefully. This could be done through repositioning approaches, saving time and cost [1].

Fig.1 "Normal ovary vs Polycystic Ovary"



2. Pathophysiology

Primary deficiencies in the hypothalamic-pituitary axis, insulin secretion and action, and ovarian function are involved in the pathogenesis of PCOS [7]. PCOS has been connected to obesity and insulin resistance, but its exact cause is uncertain. The correlation with insulin function makes sense since insulin regulates ovarian activity and when insulin levels are too high, the ovaries respond by creating androgens, which can cause anovulation [8].

Several theories have been put out to explain PCOS's pathophysiology, including:

- Endometrial progesterone resistance
- A unique defect in insulin action and secretion.
- A primary neuroendocrine defect leads to an exaggerated LH pulse frequency and amplitude.
- A defect of androgen synthesis that results in enhanced ovarian androgen production.
- An alteration in cortisol metabolism results in enhanced adrenal androgen production [9].

2.1 Endometrial progesterone resistance

Women with PCOS have lower endometrial reactivity to progesterone, and a study has found that their total endometrial progesterone receptor expression is higher. Women with PCOS have more progesterone

receptor expression in their epithelial cells than in their stromal cells, which suggests that progesterone binds less strongly to stromal cells [10].

Childhood disorders are indicative of a hereditary component. Pubertal onset could last for a maximum of two years. Onset after marriage indicates stress and obesity. And onset away from the physiological point indicates a tumor. Sclerocystic ovaries follow pelvic infection by 6-18 months [11].

2.2 Insulin resistance

It is the decreased glucose response to a certain insulin dose. Fat women and women who are not obese both frequently have insulin resistance. In PCOS, pancreatic beta-cell secretory dysfunction has also been documented in addition to insulin resistance. Insulin secretion under basal conditions rose due to a cell malfunction, while after meals, it reduced.

Two important actions of insulin contribute to hyperandrogenism in PCOS.

- Inhibition of hepatic synthesis of serum sex hormone binding globulin (SHBG).
- Inhibition of hepatic production of IGFBP-1 which allows an increased level of IGF-1 and greater local activity [9].

2.3 Neuroendocrine defect

LH hypersecretion is considered to be the primary abnormality in classic PCOS and thus cause of androgen excess [9].

2.4 Ovarian defect

PCOS is a form of gonadotropin-dependent ovarian hyperandrogenism in which the central abnormality is an elevated intraovarian androgen concentration. PCOS patients have increased formation of 17α hydroxyprogesterone and androstenedione in response to LH [9].

2.5 Increased peripheral cortisol metabolism

An increased androgen production was found in 25% of PCOS women as a result of a genetic trait or secondary to ovarian hormonal secretion. This involves irreversible inactivation of 5α reductase and 5β reductase in the liver and reversible interconversion with cortisone by 11βHSD in the liver and adipose tissue [3].

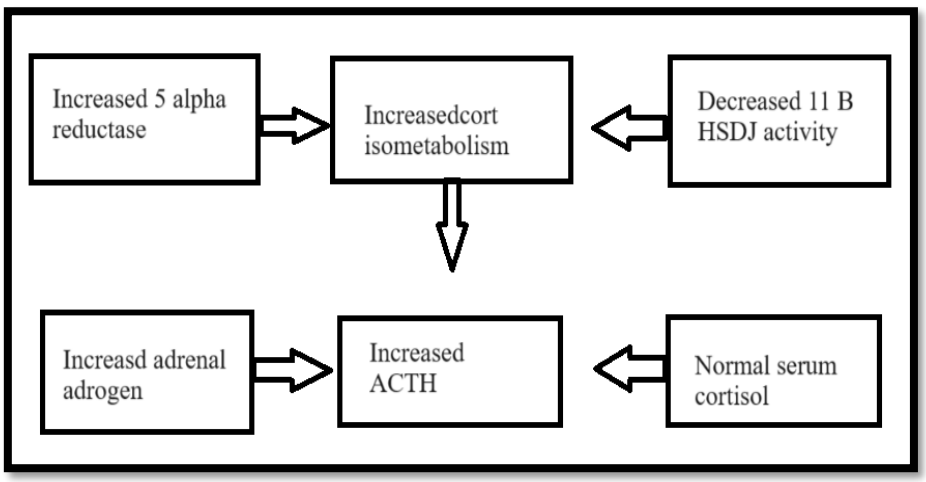
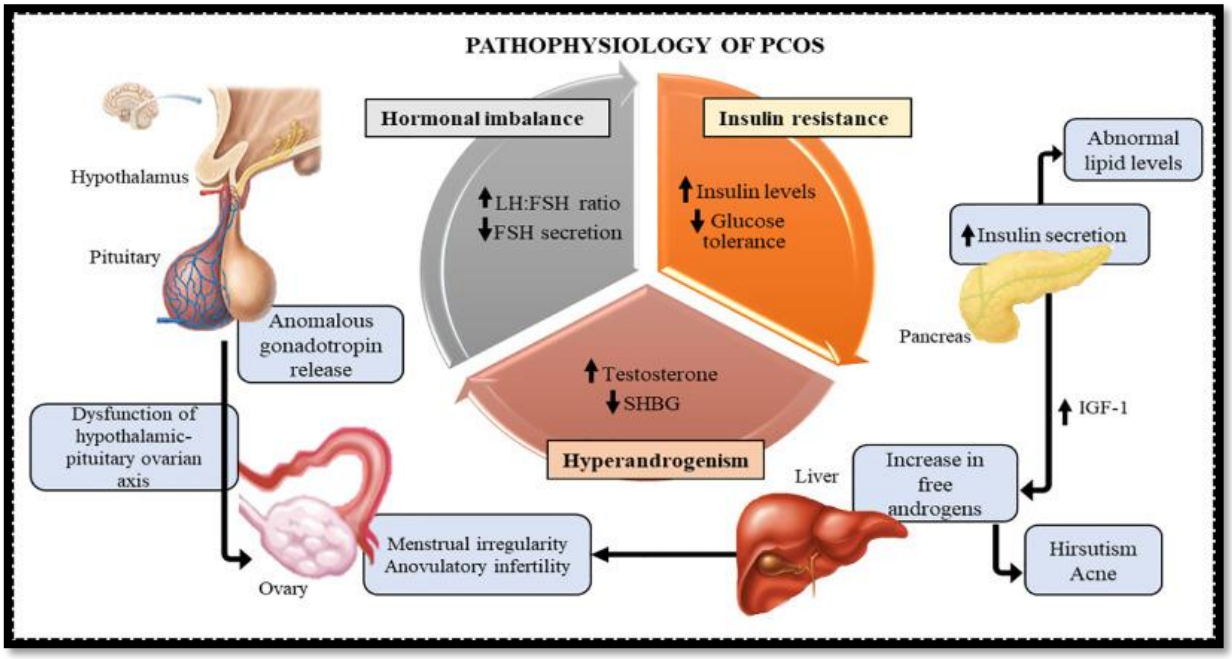


Fig.2 "Pathophysiology of PCOS"



3.Signs and Symptoms

Many symptoms contribute to PCOS such as hirsutism, acne, alopecia, acanthosis, seborrhea, infertility, insomnia, and irregular periods [12].

3.1 Hirsutism

On a woman's face and body, it is an excessive growth of hair. This condition causes unwanted hair to grow on the face, chest, and back, mostly in women, as well as on the body as a whole in men [13].

3.2 Acne

It is a chronic skin condition that causes spots and pimples. It mostly happens when dead skin cells and oil clog hair follicles, causing whiteheads, blackheads, pimples, cysts, and other skin conditions. They mainly occur on the face, shoulders, back, neck, chest, and upper arms. It may also occur due to the different peripheral sensitivity of the androgen receptors [14].

3.3 Alopecia

It is a condition in which there is sudden hair loss which leads to baldness and in this condition, there is also thinning of hair [15].

3.4 Acanthosis

It is a skin condition when there are dark velvety patches in the body folds and body creases like underarms and neck. The affected skin can become thickened and blackened [15].

3.5 Seborrhea

The condition is characterized by red skin patches, particularly on the scalp. There may be yellow plaques on the scalp. It is also a chronic inflammatory disease [15].

3.6 Striae

This is also known as stretch marks. They appear as reddened streaks on the skin it is mainly due to rapid changes in body weight or the case of pregnancy also [15].

3.7 Acrochordons

They are also known as skin tags. This is the common skin growth, which sticks out. They are small soft common benign [15].

3.8 Infertility

It is an inability to conceive after a long period of unprotected sex15].

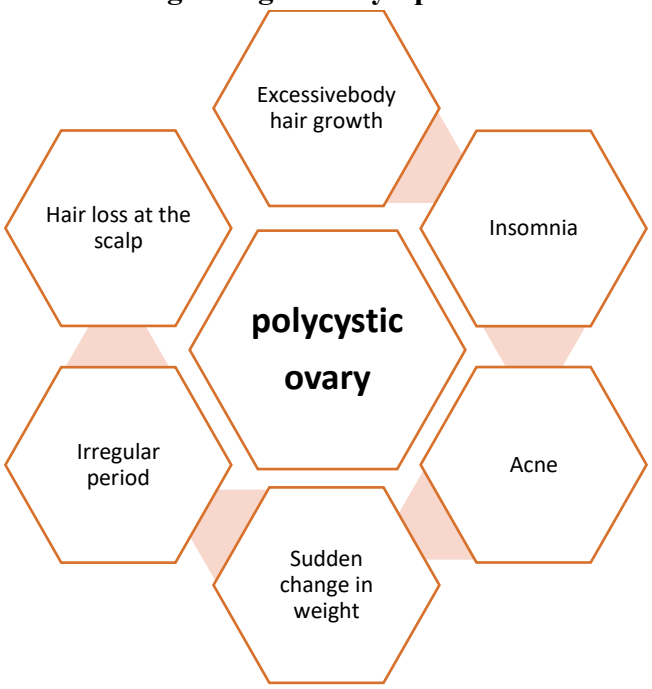
3.9 Insomnia or sleeping disorder

Women with PCOS report poor sleep or insomnia. Several factors lead to poor sleep but the PCOS is associated with a sleep disorder called sleep apnea. In the case of sleep apnea person, stops breathing for some duration during sleep [15].

3.10 Irregular periods

It is a problem with menstrual cycles. It is a condition when there are delayed, missed, or more bleeding patterns [16]. It further leads to the problem in the reproductive system. With PCOS, there is a correlation to a low level of androgen with advancing age in women [17].

Fig.3 "Sign and symptoms"



4.Causes

The exact etiology remains unknown but some of them are:

4.1 High level of insulin

Insulin is a polypeptide hormone that is produced and secreted by pancreatic beta cells. Its primary purpose is to lower blood glucose levels, which suggests that PCOS has both metabolic and reproductive morbidity [18]. The body has a lot of sugar in it if there is no insulin synthesis. It will act as a driving force for hyperandrogenism [19]. There is insulin resistance also occurring in which insulin is produced by the pancreas but our body is not able to use that insulin [20]. The ovaries produce more androgens like testosterone when insulin levels are high, which prevents ovulation [21,22]. In PCOS pregnancies, unable to prevent excess testosterone [23]. There are two potential causes of hyperinsulinemia: a rise in hyperandrogenism and a fall in the quantity of sex hormone-binding globulin in the circulatory system [24]. Black, velvety skin patches on the crotch, under the breasts, armpits, and lower neck are a sign of insulin resistance. Weight gain and increased hunger could be other indicators [25].

4.2 Environmental Pollutants

Numerous studies have demonstrated the negative effects of environmental pollutants on human health and reproduction, including heavy metals, pesticides, and endocrine-disrupting chemicals (EDCs). There is growing evidence that environmental toxins play a role in PCOS development [26]. "An exogenous agent that interferes with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and/or behavior" is what the United States Environmental Protection Agency (USEPA) defines as an endocrine-disrupting chemical (EDC). [27]. When interacting with hormone receptors, EDCs can either bind as an agonist or an antagonist. Almost everything we use on a day-to-day basis includes an EDC. They mimic the activities of steroid hormones since their structures are made of phenols or halogens like chlorine and bromine. Studies have confirmed that PCOS sufferers had higher serum concentrations of EDCs. From prenatal until adolescence, prolonged and continuous exposure to EDCs can increase a person's risk of developing PCOS [28]. An increased risk of PCOS has been linked to smoking and exposure to cigarette smoke, according to numerous research. Researchers who examined oligo-anovulatory PCOS women, women with normal PCOS anovulation, and healthy controls discovered that smoking was related in a dose-dependent manner to ovulatory dysfunction. [29].

4.3 Bad dietary choices

Eating junk food causes PCOS because junk food contains excess fat, simple carbohydrates, and sugar which leads to a high risk of obesity, Diabetes, and cardiovascular disease, which further leads to PCOS [30].

4.4 Weak immune system

Because PCOS has a low amount of progesterone, the immune system is overstimulated and produces more estrogen, which in turn triggers the production of autoantibodies. This is the most prevalent reason for irregular menstrual cycles [15].

4.5 Obesity

Because eating more junk food makes us fat and makes us more likely to get diabetes, which in turn makes us more likely to develop PCOS, obesity is the main contributing factor to this condition. Insulin resistance

and high levels of insulin in the blood, which further stimulate ovarian androgen production are associated with obesity [31].

4.6 Hormonal imbalance

The imbalance of certain hormones is common in women with PCOS.

- High testosterone level leads to hyperandrogenism.
- High LH whose excessively increased levels disrupt proper ovarian functions.
- Low sex hormone binding globulin (SHBG) allows the expression of hyperandrogenism.
- High prolactin level stimulates the production of milk in pregnancy, and it is raised in a few patients [32].

4.7 The genetic tendency for PCOS

It has been demonstrated that certain genes, gene-gene interactions, or interactions between genes and the environment may alter a person's predisposition to develop PCOS. PCOS is a polygenic and multidimensional condition. Multiple possible genes have single-nucleotide polymorphisms or mutations that have been linked to a variety of PCOS symptoms, according to several genetic research. All genes and mutations that affect the ovaries either directly or indirectly are related to PCOS [33,34]. Low birth weight and exposure to androgens during fetal development also contribute to the development of the PCOS phenotype. However, it is doubtful that PCOS represents a single gene deficiency and is more likely to be polygenic or oligogenic [35].

4.8 Inflammation and oxidative stress

Inflammation is considered one of the key features of endothelial dysfunction and atherosclerosis. In all BMI categories, women with PCOS are more likely to have significant levels of visceral adiposity. Increased blood glucose, cholesterol levels, and insulin resistance are associated with this high concentration of visceral adipocytes. These adipocytes affect endocrine as well as exocrine. Inflammation and oxidative stress are very closely interrelated. The inflammatory process generates reactive oxygen species and the oxidative stress process and products induce and aggravate inflammation. There are literature reports available that say the lipid peroxidation level increased in the case of PCOS and this rise has a positive correlation with the BMI, insulin level, and blood pressure. Additionally, there is a reduction in glutathione, haptoglobin, and antioxidants in women with PCOS. In these cases, the susceptibility towards oxidative stress-induced DNA damage also increases. Oxidative stress is also involved in many abnormalities of the reproductive system as well such as infertility, endometriosis, anovulation, and defects in the quality of oocyte [36,37].

4.9 Stress and other psychological disorders

PCOS is often caused by psychological disorders. Increased stress can upset the normal menstrual cycle and cause hormonal changes such as raised levels of cortisol and prolactin that affect menstruation that normally resumes after the stress subsides [32].

4.10 High levels of androgens

A small number of male hormones are secreted by all females, however, in PCOS patients, the ovaries release an unusually high number of androgens. When these hormones are produced in excess by the

female body, it has a deleterious impact on ovarian function.
The ovaries may not release a mature egg during each menstrual cycle if there is a hormonal imbalance of this kind. It may also affect fertility and result in irregular menstrual cycles [38].

Fig.4 "causes"

5. Diagnosis

Polycystic ovary syndrome is difficult to diagnose due to the intrinsic characteristics of the syndrome: the heterogeneity of the symptoms; and their variability in different age ranges1. PCOS is difficult or impossible to diagnose in adolescent and menopausal women because puberty mimics the signs and symptoms of polycystic ovary syndrome. It is quite simple to confuse menarche with the presence of many tiny antral follicles. In menopausal women, the recall of menses is highly inaccurate and also based on biochemical hyperandrogenaemia [39].
The basic goal of diagnosis is to detect or identify the disease by looking at its symptoms or by running numerous tests. In the case of PCOS, doctors may observe the signs and symptoms as well as do PCOS testing [40].

5.1 Appearance

The appearance of the ovaries, which are polycystic in PCOS due to the presence of more than 12 follicles, which cause the ovary to expand, is used to diagnose the condition.

5.2 Medical history

Doctors may examine a patient's medical history to diagnose PCOS, such as whether anyone else in the patient's family has the condition previously.

5.3 Symptoms

The doctor may examine all of the symptoms and indicators of that condition, including hirsutism, acne, alopecia, seborrhea, striae, acrochordons, infertility, lethargy, pelvic discomfort, mood swings, sleep issues, and irregular periods. Because PCOS is a chronic disease with increased testosterone creating problems and this hormone during pregnancy has been reported to raise the risk of neurodevelopmental abnormalities, the person with PCOS is more likely to have mental health issues including depression and

anxiety. Additionally, they could be suffering from breast cancer, diabetes, high cholesterol, hypertension, sleep issues, and heart attacks [15].

Since 1990, various bodies have laid down criteria for the diagnosis of PCOS, based on oligo or anovulation, signs of hyperandrogenism, and ovarian sonography

Criteria	NIH 1990	Rotterdam 2003	Androgen Excess Society 2006
Diagnostic criteria	Must include	Two of following three	Must include
	Chronic anovulation	1. Oligo/anovulation	Ovarian dysfunction Oligo/anovulation Polycystic ovaries on USG
	Clinical and/or biochemical signs of hyperandrogenism	2. Clinical and/or biochemical signs of hyperandrogenism	Androgen Excess Hirsutism hyperandrogenemia
		3. Polycystic ovaries on USG	

All criteria assume that other causes of androgen excess have been ruled out, PCOS: Polycystic ovarian syndrome

5.4 The Rotterdam criteria for the diagnosis of PCOS

A group of scientific experts, in 2003, elaborated the diagnostic criteria to include the ultrasound images of polycystic ovaries as another diagnostic marker and if two out of three diagnostic criteria will be met and the same endocrinopathies were excluded. This is known as the Rotterdam criteria [41]. Slowly and steadily these criteria were accepted by various societies and committees like the European Society for Human Reproduction and Embryology (ESHRE), and the American Society for Reproductive Medicine (ASRM). Although this criterion is controversial the Androgen Excess Society (AES) came up with a new set of diagnostic criteria in 2006 which are still the most commonly adopted criteria by different guidelines [42]. These guidelines are accepted and used by a wide group of obstetricians and gynecologists as well as other specialists.

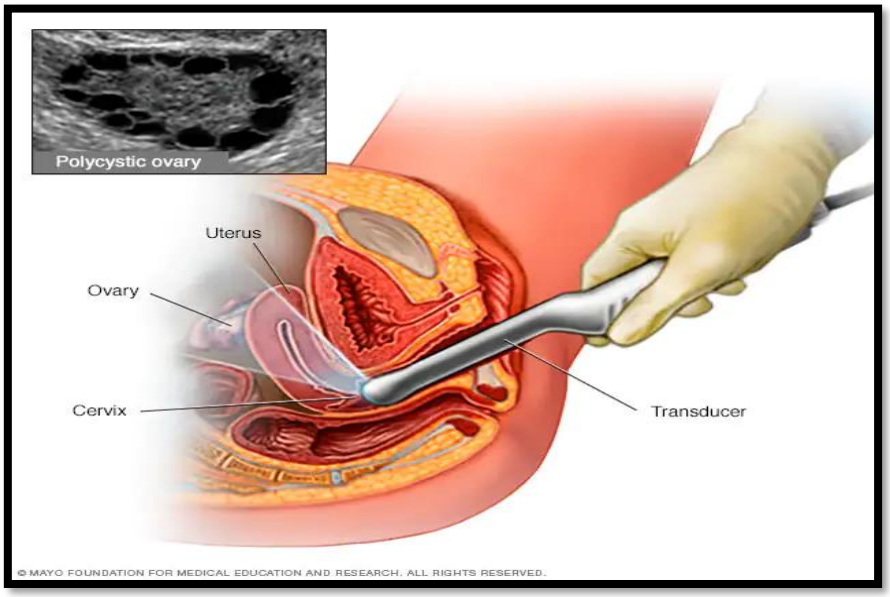
5.5 Blood test

Numerous tests are conducted to diagnose or access PCOS. Hormone levels can be measured via blood tests. With this testing, any causes of irregular periods or androgen excess that resemble PCOS can be ruled out. Additional blood tests, like fasting cholesterol and triglyceride measurements, may be performed on you. Your body's reaction to sugar (glucose) can be measured using a glucose tolerance test. Before having blood tests to determine your hormone levels, you must stop taking the contraceptive pill for three months [43].

5.6 Ultrasound

An ultrasound can check the appearance of your ovaries and the thickness of the lining of your uterus. It is a form of imaging that is used to examine internal organs and tissues. An ultrasound of the uterus, ovaries, and pelvis is advised to detect any cysts that may be present in the ovaries and to measure the size of the ovaries to determine whether they are swollen or small. Transvaginal ultrasound is a painless, radiation-free examination that is carried out on sexually active women. If necessary, an abdominal scan can be performed to determine whether the ovaries can be seen externally through the stomach walls. An ultrasonic sensor is located on the tip of a pen-shaped probe used for this form of ultrasonography. This is useful to get a clearer view than with an abdominal ultrasound [15].

Fig.3 "Transvaginal Ultrasound"



6. Treatment

Because the primary cause of PCOS is unknown, treatment is directed at the symptoms. The patient may choose not to seek therapy despite the presence of symptoms because she wants to become pregnant. Additionally, few treatment options improve every element of the illness. Reversing anovulation, preventing androgens from acting on certain tissues, and lowering insulin resistance should all be targeted treatment objectives.

Lifestyle Modification and Non-Pharmacological Approaches

6.1 Weight Loss

Women with PCOS who have elevated amounts of androgenic hormones acquire weight, primarily around the abdomen. As a result, many PCOS women have an apple-shaped body instead of a pear shape [44]. The first step for women diagnosed with PCOS would be weight reduction and calorie intake restriction [45]. Many studies demonstrate that even a 5% to 10% reduction in weight can restore the regular menstruation cycle [46]. It would be ideal for obese women to achieve their normal body mass index (BMI) range. Along with weight loss, the level of free testosterone decreases, and the incidence of metabolic syndrome reduces [47].

6.2 Diet

As was already established, the optimal dietary or nutritional plan for any woman would be one that was specifically designed to help her reach her goals. However, some recommendations might make it easier or harder to decide what to eat. A diet that is high in fiber and low in carbohydrates and saturated fats would be optimal. Low and high-glycemic-index carbohydrates are categorized according to the blood glucose response they produce within two hours. We prioritize consuming foods and vegetables with low glycemic indexes, such as broccoli, raw carrots, lentils, soy, bran morning cereals, whole-grain bread, etc. Additionally, patients should be advised that some fruits, like pineapple or watermelon, white rice, cakes, cookies, and potato chips, as well as foods with a high glycemic index, should be avoided [48,44].

6.3 Exercise

Physical activity and exercise are important for weight loss. They might help to increase insulin sensitivity. While different studies indicate different times of the week for exercise, the American Heart Association (AHA) suggests 150 minutes or 75 minutes each week for moderate to vigorous activity. Numerous studies demonstrate that exercise, in addition to a diet, can help PCOS-afflicted people resume their periods. Exercise most likely modifies the hypothalamic-pituitary-gonadal (HPG) axis, which in turn affects ovulation. Exercise causes insulin and free androgen levels to drop in overweight and obese women, which triggers the restoration of HPA regulation of ovulation. [49,47].

Pharmacological management

6.4 Clomiphene citrate

It is used as a first-line treatment for ovulation induction in PCOS patients. It is the estrogen receptor antagonist that interferes with negative feedback of the oestrogen signaling pathway resulting in increased availability of FSH. Increased FSH leads to follicular growth. It takes in the first part of the menstrual cycle. It is also used to treat infertility [50,51].

6.5 Metformin

Insulin-sensitizing agents such as metformin, and troglitazone antagonize some hyperandrogenic signs, by reducing total and free testosterone concentration. It increases ovulation reduces the problem caused by insulin resistance and regulates excessively raised levels of androgens.2 It restores the menstrual cycle, ovulation, and fertility. Metformin is a short-term treatment for PCOS that lasts three to six months and improves ovulatory functioning and androgen levels in the blood. It lowers the incidence of pregnancy-related conditions such as gestational diabetes and gestational hypertension [52,53].

6.6 Gonadotropins

It is used as a second line of therapy after resistance to clomiphene citrate. It induces ovulation and maintains and provokes optimum follicle growth with the controlled administration of FSH4 and its treatment started with low doses [54].

6.7 Glucocorticoids

Prednisone and dexamethasone have been used to induce ovulation. In PCOS patients with high adrenal androgen, low-dose dexamethasone (0.25-0.5 mg) at bedtime can be used [50].

6.8 Aromatase inhibitors (AI)-letrozole

Aromatase transforms androgens into estrogen. The most popular non-steroidal selective AI for inducing ovulation in the third generation is letrozole. The ovarian production of estradiol is inhibited by letrozole. Increased FSH secretion by the pituitary increases the ovulation rate via enhancing follicular sensitivity to FSH. This is because the ovary experiences a brief increase in androgens and the brain releases negative feedback [55].

6.9 Oral contraceptives

The main way that oral contraceptives (OCs) work to treat PCOS is by controlling menstruation. These medications also lower testosterone levels, which reduces hirsutism, acne, and other related issues. The

most popular over-the-counter (OC) treatments for PCOS-related hirsutism and acne are combinations of estrogen and progestogen. Theoretically, these drugs work better than earlier formulations to treat androgenic symptoms [56,57].

6.10 Insulin sensitizing agents

PCOS patients have abnormal insulin function and secretion. It has long been recognized that hyperinsulinemia and insulin resistance in PCOS patients result in increased testosterone levels. Ovarian function is regulated by insulin, and elevated insulin levels may be detrimental to the ovaries. Large amounts of androgens are released by muscle cells in response to high insulin levels, which delays follicular development and results in the polycystic ovarian shape that is a defining feature of PCOS. Acanthosis nigricans has historically been used to indicate insulin resistance. Insulin resistance makes PCOS patients more vulnerable to chronic health issues like type 2 diabetes and cardiovascular disease, both of which have a high death rate. Therefore, managing insulin resistance with drugs and changing one's lifestyle is crucial for PCOS treatment [58,59].

6.11 Vitamin D

A growing body of research indicates that PCOS can develop during a woman's reproductive years, can occur during pregnancy in genetically predisposed individuals, and can manifest clinically during adolescence. Between 45 and 90 percent of women who are of reproductive age suffer from inadequate or insufficient vitamin D. Studies have shown that a shortage in vitamin D was associated with a significant reduction in the frequencies of ovulation, pregnancy, and live birth in PCOS patients. patients with female infertility receiving ovarian stimulation. Vitamin D therapy may be beneficial for patients with metabolic problems, ovulation dysfunction, and polycystic ovarian syndrome [60,61,62].

6.12 Antiandrogens

Antigens such as finasteride, spironolactone, and flutamide help PCOS patients with their acne and hirsutism. These antigens may be helpful for those with elevated lipid levels, which are common in PCOS patients. The effects of finasteride (5 mg), flutamide (250 mg), and spironolactone (100 mg) were investigated in 40 hirsutistic women over six months [63].

6.13 Statin

Statins are believed to have a role in the treatment of PCOS because of their ability to reduce testosterone levels, triglycerides, low-density lipoprotein cholesterol (LDL-C), and total cholesterol. In women with PCOS, metformin, and simvastatin (Zocor, Merck) reduced total testosterone levels by 13.6% and 17.1%, respectively. Simvastatin performed better than metformin alone, although the combination was not found to be 15.1% more effective than simvastatin alone. [64,65].

6.14 Surgery

Androgen-producing tissues are destroyed during laparoscopic ovarian drilling (LOD), which is utilized in patients who do not react to clomiphene treatment. reestablishing ovarian function and addressing the hormonal imbalance. To treat acne and hirsutism, hyperandrogenism is suppressed [66,67].

Ayurvedic management of PCOS

6.15 Satapushpa churna

Seeds of the satapushpa plant (Foeniculum vulgare mill) are a useful addition to PCOS treatment. Their phytoestrogen content is high. The phytoestrogens in fennel contribute to lowering PCOS inflammation and insulin resistance. It's also thought to lessen the cellular imbalance that causes PCOS's metabolic problems [68].

6.16 Shatavari churna

In Indian medicine (ayurveda), asparagus racemosus (wild) (Asparagaceae) is traditionally employed. Because of its phytoestrogen (natural estrogen derived from plants), it helps to promote the correct growth of ovarian follicles, regulates the menstrual cycle, and revitalizes the female reproductive system. It also aids in the fight against hyperinsulinemia [69].

6.17 Dashamularishta

Dashamularishta is a traditional Ayurvedic polyherbal composition made from powdered herbs and a natural fermentation process of decoction. In addition to a collection of ten herb roots called dashamula, it has more than fifty herbs. In Vatasaman, therapeutic purposes are mentioned. Ayurveda states that Vata is a major factor in the vitiation of all ailments linked to women. Therefore, Dashamularishta is very important for suppressing vata. It has been mentioned in the Sharangadhar Samhita regarding infertility [70].

6.18 Sadavindu taila

Used as naya, sadavindu taila travels via the nasal canal to reach shringataka Marma (siro Antarmadhyam). It covers the entire region of Urdhwajatrugata. The morbid Doshas are eradicated by it. It activates the neuron that releases gonadotropin (GnRH). As a result, it controls the pulsatile release of gonadotropin-releasing hormone. Eventually, it causes ovulation, which resolves PCOS symptoms [70].

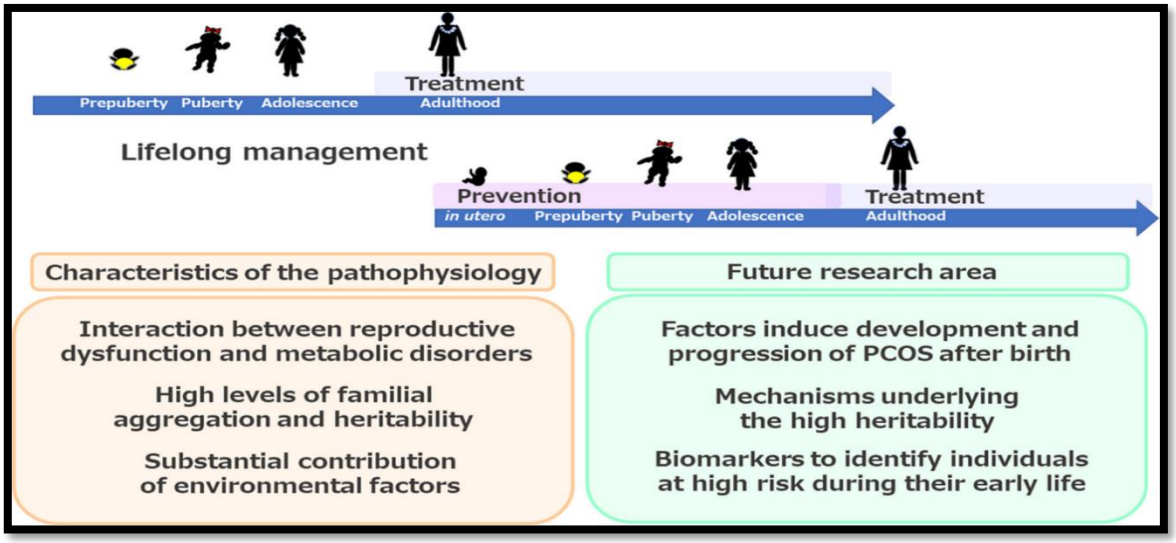
6.17 Aaroghyavardhini Vati

Aaroghyavardhini vati aids in "prasadbhuta raja nirmitee," or the production of excellent follicles, by acting on rasa and rakta dhatu. It boosts "kayagi" and "dhatwagni," or the liver's secretions of sex hormone-binding globulin, which lowers the production of androgens. This is achieved by stimulating the liver's activities. One of the main ingredients of Aroghyavardhini vati is kutaki (picrorhiza kurroa Royle ex Benth), which is pitta virechak. Rakta suddhi follows. In the end, Artavavaha Srotas's suddhi happens [70].

7.Future perspective

Based on this current understanding, the following three areas represent targets for future research. First, it is important to pinpoint the triggers for PCOS's onset and advancement and to clarify the underlying processes. The mechanism linking the metabolic and reproductive problems that make up the pathophysiology of PCOS is particularly interesting, as it may be utilized to target the disruption of the vicious cycle involved. However, there hasn't been much study done in this area up to this point. Furthermore, additional research is required to understand how environmental factors including lifestyle choices and the follicular microenvironment influence the development of PCOS through effects that

manifest after birth. Moreover, the discovery of new variables, some of which might be psychological in nature, will broaden our knowledge of the pathophysiology [71].



Clarifying the processes behind PCOS's high heredity is the second topic that needs more investigation. The role of genetic factors may have been understated in the study conducted thus far. The "common disease, common variants" theory behind GWAS, which states that the small number of common variants with moderate-to-low effect sizes that can be found using this method cannot explain the etiology of common and complex diseases, may be partially responsible for the limited contribution of the genetic loci found by GWAS [72]. The examination of gene-environment interactions and other innovative approaches, when combined with GWAS, may provide light on the precise roles played by genetic variables in the high heritability and family aggregation of PCOS [71].

Research on the processes by which the intrauterine environment during the perinatal period predisposes to the development of PCOS in later life is still in its infancy, but it is a promising field given the growing body of evidence suggesting that this phenomenon affects people as well as experimental animals. As mentioned, research is necessary to determine whether dysbiosis of the offspring's gut microbiota and the activation of epigenetic modifications in fetal somatic and/or germ cells occur. As it relates to the gut microbiome, determining which amounts of fecal metabolites are impacted by dysbiosis and investigating the connections between the gut and other organs could enhance our comprehension of the pathophysiology of PCOS as a systemic illness.

The third area of research that has to be done is the identification of biomarkers that may be utilized to identify individuals early in life who are at high risk of developing PCOS later in life. A statewide register-based cohort study conducted in Sweden found that among the daughters born to PCOS-positive mothers, just 3.3% (78/2275) developed PCOS in the future, while the remaining 96.7% did not. Women who are born to mothers who have PCOS are significantly more likely to also develop PCOS. In individuals who are supposedly at low risk, like those who were born to moms without PCOS, biomarkers that can be used to detect women who are predisposed toward the development of PCOS might also be beneficial. It may be possible to identify daughters who are at high and low risk by evaluating the mother's metabolic and/or hormonal status during pregnancy. In contrast, a biomarker that can identify females who may go on to develop PCOS in the future could be found in their metabolic and/or hormonal condition throughout their early years of life, such as infancy or childhood. Future studies should pay particular attention to completely novel indicators, such as gut microbial makeup or fecal metabolites [73].

Conclusion:

PCOS is a treatable illness that necessitates a specific strategy for therapy. With an emphasis on enhancing general health and well-being, people with PCOS need to collaborate closely with their healthcare professionals to develop a customized strategy that addresses their unique symptoms and objectives. The quality of life for PCOS patients can be greatly enhanced by an early diagnosis and prompt treatment.

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