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POLYCYSTIC OVERY SYNDROME: AN EXAMINATION OF CLINICAL CHARACTERISTICS AND DIAGNOSTIC STANDARDS

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Abstract

Hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology—a prevalent endocrine and metabolic disorder—are the hallmarks of PCOS. One of the main causes of infertility in women of reproductive age is PCOS, which affects up to 12% of women. This review explores its intricate genesis and pathophysiology, paying special attention to the roles of inflammation, insulin resistance (IR), and hyperandrogenism. We look at current and historical diagnostic criteria (NIH, Rotterdam, AE-PCOS) and the challenges they pose for adolescents and other populations.Briefly, management measures include reproductive options, pharmaceutical therapy (metformin, OCPs, and anti-androgens), and lifestyle changes. Cardiovascular and metabolic diseases are among the long-term health concerns that should be reduced by early detection and optimized, comprehensive assessment.

1.Introduction

Women between the ages of 15 and 49 who are in their reproductive years are susceptible to PCOS, also known as polycystic ovarian syndrome, a common ring gynecological disease [1-2]. Polycystic ovarian syndrome (PCOS), also referred to as hyperandrogenic anovulation of reproductive age or Stein-Leventhal syndrome worldwide, is a multifactorial and polygenic endocrine disease that affects women [3]. Polycystic ovarian syndrome (PCOS) is a complex endocrine disorder that impacts a woman's metabolic and reproductive systems, among other aspects of her health. Given that 12% of people worldwide have PCOS, the most recent international standard, which was updated in 2023, updated the diagnostic and PCOS management guidelines due to the fact that there have been numerous definitions of PCOS throughout history [4]. There are other contributing factors, and scientists are still studying the pathogenesis, environmental and genetic variables, steroidogenesis disruption, metabolic or neuroendocrine changes may be responsible for the development of this syndrome [5]. Elevated levels of Folli statin, which is associated with PCOS as well as other conditions that accompany it, such as type II diabetes, are also important [6]. Three key concepts underlie the female metabolic disease known as polycystic ovary syndrome, or "PCOS": amenorrhea, ovulatory dysfunction (OD), which frequently presents as irregular menstruation or morphological polycystic ovaries (PCOS), and clinical and biologic hyperandrogenism (HA). The majority of research indicates that it affects between 2% and 40% of women who are of reproductive age and, more frequently, between 6% and 13% of women in general. The estimated prevalence rate may vary based on the study method, ethnicity, diagnostic criteria, and other factors, but it is one of the primary but treatable causes of infertility [7–8]. Patients should keep an eye on their health and take precautions to avoid the

development of related disorders. Among the most effective and economical methods of treating PCOS are a nutritious diet and consistent exercise [9].

The development of multiple cysts in the ovarian follicles due to a hormonal imbalance is known as PCOS. The ovary enlarges to a width of 10 cm as a result of the water-retained cysts, some of which can be as wide as 10 mm. Pregnancy becomes challenging when ovulation and the menstrual cycle are absent because they hinder fertilization and conception [10-11]. Although the precise origin of PCOS is yet unknown, it is thought to be a complex illness. PCOS has been associated with genetic anomalies related to steroid production. It is believed that these genetic predispositions may interact with environmental variables, like obesity or insulin resistance, to contribute to the condition's beginning or development. An overabundance of androgens is the fundamental mechanism behind PCOS. Functional ovarian hyperandrogenism (FOH), which is found in the majority of PCOS patients, is typified by a heightened gonadotropin-induced release of 17-hydroxyprogesterone. Excess insulin is believed to be a possible underlying mechanism of FOH, as it impairs the ovaries' ability to respond to luteinizing hormone (LH), Which results in regulation of the ovarian cycle. Increased LH levels can aggravate PCOS symptoms due to increased androgen production. Overproduction of insulin and androgens may result in premature granulosa cell development and over-recruitment of primordial follicles, leading to increased production of estrogen by these cells [12].

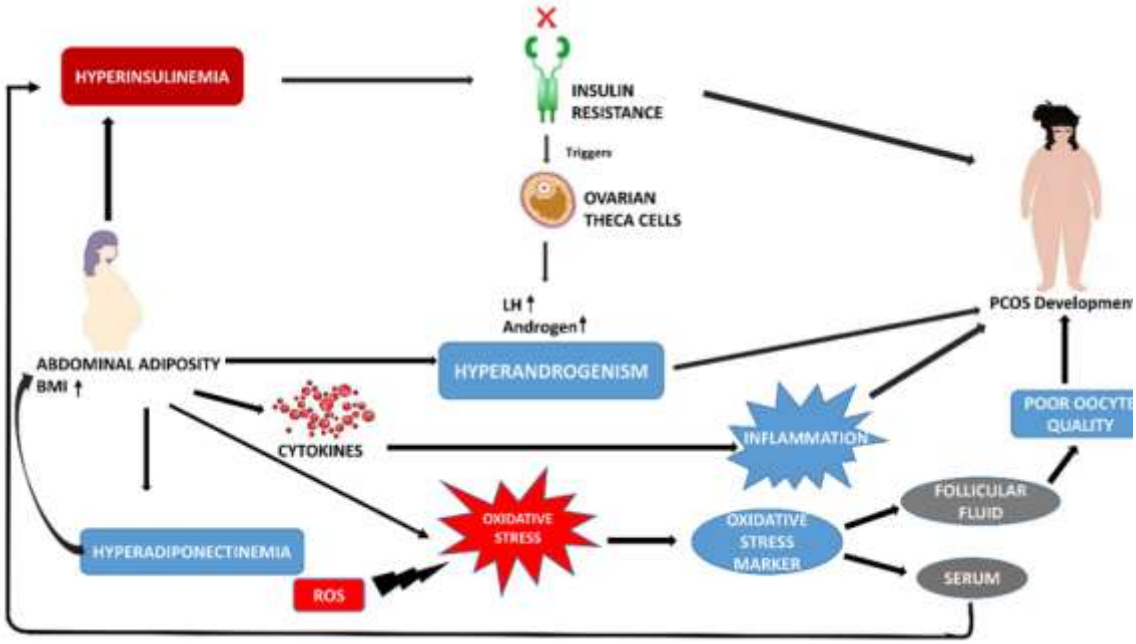

Figure 1: - Oxidative stress, inflammation, hyperandrogenism, abdominal obesity, and hyperinsulinemia all contribute to the development of PCOS. Hyperandrogenism is the result of ovarian theca cells producing more androgens due to insulin resistance caused by chronic hyperinsulinemia. Furthermore, oxidative stress, cytokine release, and hyperandrogenism brought on by abdominal obesity lead to inflammation and poor ovulation quality. (21)

2. Risk Element

A woman's risk of developing PCOS is increased by the following risk factors. These factors influence and are connected to secondary problems like diabetes, high blood pressure, and type 2 uterine cancer.

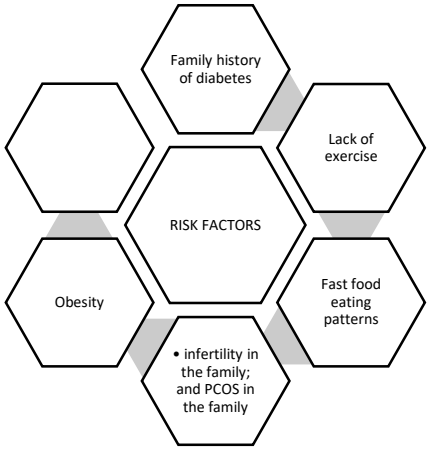

Figure 2: showing risk factors of PCOD

3.Diagnostic Criteria for PCOS

PCOS can be defined by some clinical criteria, although the most relevant criteria for PCOS diagnosis are still up for debate. In 1935, Stein and Leventhal were the first to describe PCOS as an endocrine disorder that results in oligo-ovulatory infertility in females. Despite being the most widely used PCOS classification, the Rotterdam 2003 criteria are not universally recognized. Most scientific bodies and health authorities currently recognize three criteria for PCOS [15]. The National Health Service (NHS) states that irregular or infrequent cycles, elevated androgen levels, or hyperandrogenism symptoms (acne, alopecia, hirsutism), and pictures of polycystic ovaries serve as specific standards for PCOS diagnosis [16]. The most widely used PCOS diagnostic technique at this time is the Rotterdam diagnostic criteria, which identify the existence of at least two clinical or biochemical signs of polycystic ovaries, ovarian failure, or hyperandrogenism [17].

3.1 NIH Standards

In 1935, Stein and Leventhal were the first to report seven female patients who had symptoms of the disease that later became known as PCOS. But the National Institute of Child Health and Human Development did not attempt to do so until 1990. Give a more detailed description of PCOS [22]. In 1990, the NIH was the first body to create formal, standard diagnostic criteria, and according to these guidelines, the prevalence rate of PCOS is between 5 and 8%. Two traditional conditions are recommended by the NIH for the treatment of PCOS, which are characterized by biochemical or clinical signs of hyperandrogenism as well as irregular or missing ovulation/menstruation (OD). Pelvic imaging of polycystic ovaries is not an essential NIH requirement as not all women with other PCOS symptoms have it, but women must be diagnosed with both abnormalities to be diagnosed with PCOS [23]. Therefore, in 2012, the NIH held an Evidence-Based Practice PCOS Workshop, which addressed the topics while also addressing the “benefits and shortcomings” of current diagnostic criteria [24]. The meeting was conducted in compliance with general NIH standards for consensus development programs, and 29 PCOS experts presented all relevant evidence.

3.2 Rotterdam criteria

In 2003, the Rotterdam Consensus Workshop determined that the primary characteristics of PCOS were insulin resistance, irregular menstruation, and hyperandrogenism [25–26]. Experts met in Rotterdam, the Netherlands, in 2003 and came to a "Rotterdam Consensus" on the diagnosis of PCOS. This consensus became known as the "Rotterdam Criteria," and it is still the most widely used and advised recommendation. The Rotterdam Criteria have actually been used extensively in the last 20 years [27]. The Rotterdam Criteria were created to broaden the definition of PCOS and include the NIH criteria. According to the Rotterdam Criteria, up to 15% of women of reproductive age have PCOS [28–29].

3.3 AE-PCOS

The androgen excess society, which is now called the androgen excess-pcos society [ae-pcos], put together another expert task force in 2006. [30]. It is also important to rule out other illnesses or conditions that might mimic PCOS, such as non-classic adrenal hyperplasia with 21-hydroxylase deficiency, androgen-secreting neoplasms, androgenic/anabolic drug use or abuse, Cushing's hyperandrogenic-ir-acanthosis syndrome, hyperprolactinemia, thyroid issues, and nigricans syndrome. [33]. According to the Rotterdam criteria, the prevalence rate of PCOS is either slightly lower or comparable to that found using the ae-pcos criteria [32–33].4. Diagnostic challenges in adolescents and different ethnicities of pcos

4.1. Diagnostic Challenges in Adolescents

Diagnosing polycystic ovary syndrome (PCOS) in teens can be challenging because many of the typical physical symptoms of puberty can be mistaken for PCOS symptoms.
One. Overlaps with normal pubertal changes: The HPO (hypothalamic-pituitary-ovarian) axis is immature during the first few years after menopause, leading to irregular menstruation, acne, and mild hair loss. These features may be mistaken for PCOS, potentially resulting in overdiagnosis [35–36] . B. Criteria for Menstrual Irregularity It is common for irregular periods to persist for two to three years after menstruation. A cycle lasting more than 45 days after menstruation and continuing for more than two years is more suggestive of PCOS [37]. C. Assessment of Hyperandrogenism Acne and hirsutism are examples of clinical hyperandrogenism, which is subjective and typically coincides with puberty. Although biochemical hyperandrogenism, or increased total/free testosterone, is more reliable, laboratory reference ranges for adolescents are not well defined [38]. D. Ovarian Morphology on Ultrasound Due to the prevalence of multifollicular ovaries in adolescents, polycystic ovarian morphology (PCOM) is not recommended as a diagnostic criterion. Before eight years after menarche, the Rotterdam requirements do not apply [39]. Since most diagnostic systems (NIH, Rotterdam, AE-PCOS) were created for adults, there are conflicting diagnoses in young girls [40–41–42].

4.2. Diagnostic Difficulties in Various Ethnic Groups

Due to genetic, environmental, and cultural variables, PCOS presentation varies by ethnicity, making diagnosis and treatment more difficult. One. Clinical Presentation Variations A. Women from South Asia and the Middle East are more likely to have hirsutism, insulin resistance and metabolic problems. East Asian women: greater metabolic risk and irregular menstruation, but lower testosterone levels and hirsutism are intermediate features of Caucasian women [43]. B. Biochemical and hormonal variability: Because lipid/glucose profiles and testosterone levels vary between ethnic groups, standard cut-off values may not be applicable everywhere [44]. C. Metabolic risk and body composition: Obesity thresholds and BMI vary by population. For example, Asians are more likely than Europeans to develop insulin resistance at low BMI [45]. D. Genetic and environmental factors: Dietary practices, lifestyle changes, and genetic predispositions all influence biochemical outcomes and symptoms [46]. Barriers to healthcare and cultural access. In some cultures, the stigma associated with menstrual or reproductive problems may delay diagnosis. Differing health care resources and lack of awareness also complicate diagnosis [47].

4.3. Summary Table

Area of Challenge	Teenagers	Different Ethnic Groups
Pattern of Menstruation	PCOS is mimicked by pubertal irregularities	Diet and lifestyle have an impact on cycles.
Hyperandrogenism	Undefined; lacks conventional lab ranges+	varies in appearance and severity
Ultrasound	Untrustworthy before eight years after menarche	Ethnic differences exist in ovarian size.
Risk of Metabolic	It's challenging to evaluate	Various BMI cutoff points

	early	
Diagnostic and Cultural	Absence of criteria for adolescents	Non-ethnicity-specific guidelines

TABLE NO 1: Summary table of Diagnostic Difficulties in Various Ethnic Groups

5.Sign and symptom's

Oligo-ovulation or anovulation is among the most prevalent signs of PCOS, or polycystic ovary syndrome.. Some women suffering from excessive androgen production from ovarian cysts develop virilization, or the development of more masculine characteristics. Weight gain, increased subcutaneous and abdominal fat, hirsutism (excess hair on the body and face), Among the male-like symptoms that manifest as PCOS are male-pattern alopecia (hair loss), clitoromegaly (enlargement of the clitoris), deepening of the voice, seborrhea (oily skin), and acne. [48] Individual differences in PCOS symptoms are significant, and not all patients exhibit all features of the condition. Low fertility and irregular menstruation, often manifested as amenorrhea (absence of menstruation) or oligomenorrhea (fewer menstruation), are the most prevalent symptoms and complications. These menstrual irregularities result in infertility or difficulty conceiving in approximately 73–74% of cases [49–51]. Another characteristic symptom of PCOS is hirsutism, which results in excessive facial, chest, and back hair growth. or abdomen in 85-90% of women due to high testosterone levels. Along with baldness, receding hairline, sticky skin and hair, and sometimes a deep or soft voice, acne is also common, especially during adolescence [52–53].

PCOS has a complex etiology that involves a mixture of lifestyle, environmental, and genetic variables. This condition can arise as a result of endocrine abnormalities such as Cushing's syndrome, Thyroid, Cushing's syndrome dysfunction, malfunction, tumours that secrete androgens, and hyperprolactinemia. Furthermore, the pathophysiology of PCOS may be influenced by congenital adrenal hyperplasia and disorders associated with increased cortisol levels. Additionally, there is increasing evidence that chemical exposure significantly contributes to the development of PCOS. Women in modern life are regularly exposed to a variety of chemicals, either intentionally through the use of cleaning supplies, cosmetics, and medications, or unintentionally through the use of pesticides, industrial pollutants, and vehicle emissions. One of the main reasons for the increased prevalence of PCOS is thought to be the widespread use of personal care items, including hair dyes, sunscreens, deodorants and perfumes, which are now essential parts of everyday care [54].

Additionally, PCOS clinical signs include

- Excessive weight gain: Although some PCOS-affected women may be of normal weight, being overweight can exacerbate PCOS symptoms, raise the risk of metabolic problems, and impair fertility. Obesity and overweight affect 40-60% of women with PCOS, increasing the risk of heart disease and causing metabolic abnormalities. Additionally, PCOS clinical signs include
- Body form changes
- high blood pressure
- elevated blood sugar levels [49-50-55-56].

6.Etiology and pathophysiology

PCOS has a very complex pathophysiology involving many variables including hormonal imbalance, insulin resistance, anomalies in metabolism and hyperandrogenism. There are many both recognized and unidentified reasons. There are many causes of PCOS, in addition to a a variety of symptoms and indicators, and other medical conditions. The complexity of this problem is represented by the existence of a specific disease called Polycystic Ovarian Disorder (PCOS), which PCOS is a problem, malfunction in the ovarian cells, namely theca cells, is the main cause of PCOS. This abnormality causes the biochemical and clinical signs.of the disease due to excessive production of androgens. Ethnicity is one of the genetic factors that has been linked to the development of PCOS; Mexican, Native American, and Spanish women are more likely to have this condition [57–58]. Increased LH-dependent ovarian testosterone (T) synthesis, elevated The relationship between follicle stimulating hormone (FSH) and luteinizing hormone (LH) release, repeated

Obesity, significant insulin resistance, dysglycemia, and excess adrenal androgen are the hallmarks of PCOS [59].

The information below indicates that the development of metabolic and reproductive problems is dependent on increased LH levels. LH initially promotes the synthesis of aetiology, the branch of medicine that investigates the origins and causes of diseases. In addition to environmental factors, it may also involve genetic or hereditary factors. Over time, a number of theories have been put forth to explain the pathophysiology of PCOS. At first, it was believed that this illness could be caused by an excess of intrauterine androgen. Thus, PCOS and hyperandrogenism may develop as a result of insulin resistance [62].

6.1 ETIOLOGY OF PCOS

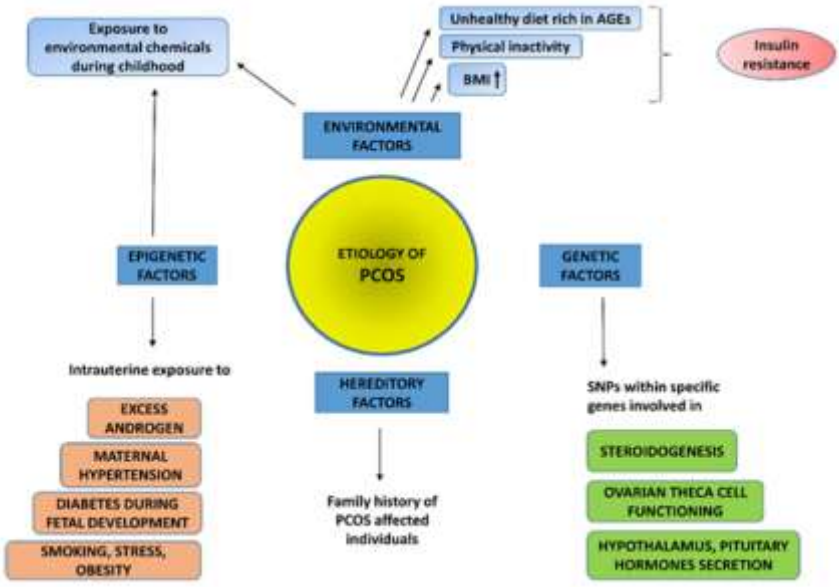

Figure 3: Factors that contribute to PCOS development [63]

6.2 Pathophysiology of PCOS

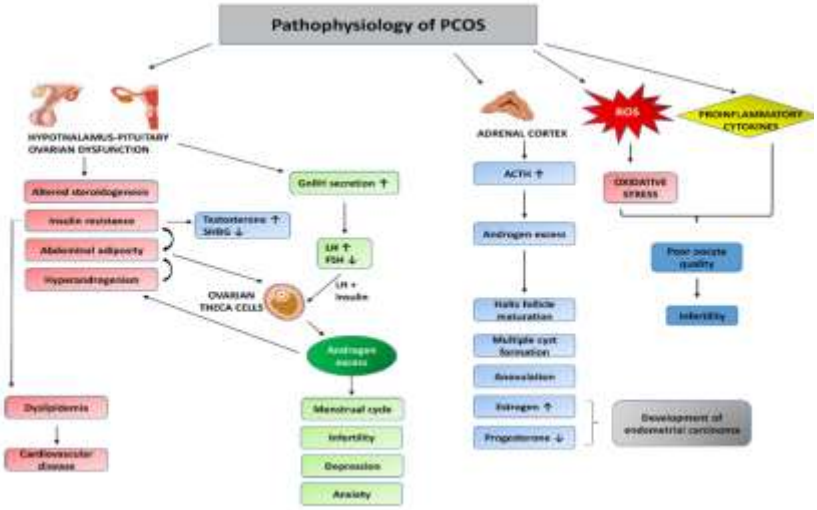

Figure 4: Reflects the pathophysiological mechanisms of PCOS, including abnormalities in the adrenal cortex, hypothalamic-pituitary-ovarian axis, increased oxidative stress, and pro-inflammatory cytokines (63).

7.INSULIN RESISTANCE AND PCOS

Insulin can regulate glucose It is estimated that insulin resistance (IR) affects approximately 75% of PCOS patients. [64]. Balance by inhibiting glucose synthesis in the liver [65] or stimulating Insulin-responsive target tissues that absorb glucose include skeletal muscle, cardiac muscle, and adipocytes. Furthermore, insulin prevents lipolysis, which lowers blood levels of free fatty acids and may mediate the effects of insulin on hepatic glucose production [66]; Nevertheless, insulin has additional metabolic, mitogenic, and reproductive functions [67].

As was previously mentioned, hypothalamic POMC neurons express both insulin and leptin receptors. Eliminating these receptors in POMC neurons caused the PCOS phenotype, indicating that insulin and leptin may be powerful regulators of kisspeptin and POMC neurons, further promoting the development of PCOS (70). Insulin works in many different parts of the body. The liver, fatty tissue, and skeletal muscle are the primary targets. As a tissue that absorbs glucose, skeletal muscle requires energy to remain functional. A rodent model has been used to explain the significance of myocyte insulin receptors. For instance, muscle-specific insulin receptor deletion mice showed signs of obesity, dyslipidemia, reduced glucose absorption, and glycogen synthesis, although it is unclear whether this would lead to hyperinsulinemia or high blood sugar. On the other hand, comparable studies in liver tissues of rodents lacking the insulin receptor show a more noticeable increase in the release of insulin and higher amounts of glucose. Additionally, Adipose tissue is extremely sensitive to insulin, which acts primarily through the PI3K-AKT pathway [71]. Although obesity can worsen insulin resistance, cause adipocyte dysfunction, and increase androgen excess in PCOS patients, insulin resistance is a Resistance to insulin is a major pathophysiological feature of PCOS and occurs regardless of obesity [73].

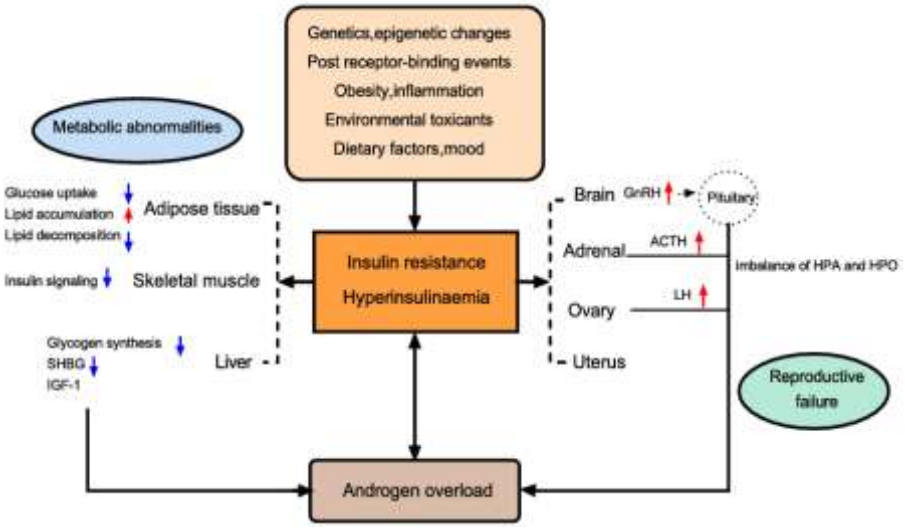

Figure 5: An overview of the most typical consequences of IR and HI in PCOS-affected women. Shorthand Gonadotropin-releasing hormone (GnRH), adrenocorticotropic hormone (ACTH), hypothalamus-pituitary-ovary (HPO), hypothalamus-pituitary-adrenal (HPA), luteinizing hormone (LH), insulin growth factor 1 (IGF1), and sex hormone-binding globulin (SHBG) [82].

7.1 pathways of insulin resistivity in patients with pcos

Insulin resistance is one of the primary characteristics of PCOS (IR), which affects the liver, adipose tissue, skeletal muscle and ovarian theca/granulosa cells. This is known as "selective insulin resistance" because ovarian insulin signaling for androgen synthesis is unaffected by systemic IR. Causes hyperinsulinemia, which aggravates anovulation and hyperandrogenism [74].

7.2 Molecular Pathway

Step 1: Insulin Binding

Insulin binds to the cell membrane through the insulin receptor (IR). PCOS is characterized by serine IR and insulin receptor substrate-1 (IRS-1) phosphorylation rather than specific tyrosine. This alteration reduces both receptor activity and signal transduction efficiency [75].

Step 2: Impaired IRS–PI3K–AKT Pathway

IRS typically initiates the phosphatidylinositol-3-kinase (PI3K) → protein kinase B (AKT) pathway Defective IRS-1 reduces PI3K activation in PCOS, resulting in reduced AKT phosphorylation (p-AKT).In Skeletal muscle and fat, reduced glucose absorption results from decreased translocation of GLUT4 crosses the membrane of the cell [76]

Step 3: Increased Serine Kinase Activity

Serine kinases (e.g., JNK, IKKβ, mTOR, PKCθ) are activated by inflammation, free fatty acids, and androgens. By phosphorylating IRS-1 on serine residues, these kinases inhibit insulin signaling and lead to insulin resistance [77].

Step 4: PI3K Pathway Dysfunction Leads to Metabolic Effects

GLUT4 translocation → PI3K–AKT signaling → ↓ glucose uptake → elevated blood sugar levels Failure Inhibiting gluconeogenesis in the liver reduces hepatic glucose production. The lack of suppression of lipolysis in adipose tissue results in the formation of free fatty acids [78].

Step 5: Selective Insulin Sensitivity in Ovaries

Insulin continues to trigger the mitogen-activated protein kinase (MAPK) pathway in theca cells.This increases the expression of steroidogenic enzymes (CYP17A1), resulting in increased androgen production. Therefore, steroidogenic actions are preserved while metabolic insulin actions are affected [79].

Step 6: Hyperinsulinemia Feedback Loop

To compensate for IR, pancreatic β-cells release more insulin. Elevated insulin: Increases androgen production by the ovaries. Increases free androgens by suppressing sex hormone-binding globulin (SHBG). Makes anovulation and follicular arrest worse [80].

8.Source of Excess Androgen in PCOS

PCOS traditionally shows that in adolescents with PCOS, menstrual disruption and hyperandrogenism are interconnected and occur simultaneously. A condition known as hyperandrogenism develops as a result of excessive production of androgens by the ovaries and adrenal glands during puberty. Acne, hirsutism, alopecia, central obesity, and acanthosis nigricans – a pigmentation of the skin marked by thick, dark spots that form in skin folds and folds – are the primary clinical symptoms indicating hyperandrogenism. The hormones that circulate in female blood are known as androgens and include dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulphate (DHEAS), testosterone (T), dihydrotestosterone, and androstenedione (A). The order of their serum concentrations is decreasing [83]. However, the ovaries' overproduction of androgens is a significant contributing element to the development of PCOS. In the sections that follow, we will examine the cellular impacts of androgen production mechanisms, particularly in the ovaries of PCOS-affected women [84]. AR, androgens contribute to the pathophysiology of PCOS through both extraovarian and intraovarian pathways. According to reports, the ovaries, skeletal system, and hypothalamus all exhibit hyperactivation of AR, adipose, and muscle cells in women with PCOS [85].

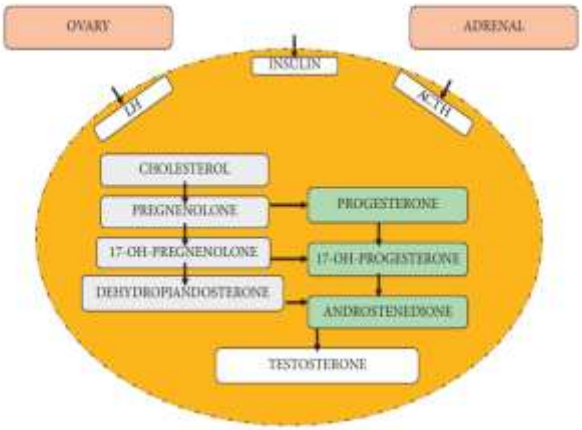

Figure 6: The adrenal glands and ovaries produce androgens. Androgen production associated with adrenal glands and ovaries [87.]

8.1. Mechanisms Synopsis (Flowchart) androgen production

Increase insulin and LH

↓

Stimulation of theca cells

↓

The activity of CYP17A1

↓

Increase androstenedione and testosterone

↓

Imbalance in SHBG (caused by insulin)

↓

Increase Testosterone that is free

↓

Clinical Hyperandrogenism in PCOS + Peripheral 5α-reductase activity

↓

Increase DHT + Adrenal hyperactivity (↑ ACTH response) → ↑ DHEA / DHEAS [91-92-93-94].

One of the main characteristics Excessive androgen production is a symptom of polycystic ovarian syndrome (PCOS), or hyperandrogenism, which causes hirsutism, acne, alopecia, and irregular menstruation, among other clinical symptoms.

8.1 Sources of Excess Androgens in PCOS

• Source	• Principal Hormones Generated	• involvement in PCOS
• Theca cells in the ovaries	• Dehydroepiandrosterone (DHEA), androstenedione, and testosterone	• main cause of most PCOS women's high androgens
• Zone reticularis, or the adrenal glands	• Androstenedione and dehydroepiandrosterone sulphate (DHEAS)	• secondary source; in about 20–30% of cases, it helps
• Adipose, skin, and other peripheral tissues	• Androstenedione conversion to testosterone and then to dihydrotestosterone (DHT)	• Increases local androgenic effects; minor but clinically significant

TABLE 2: Sources of Excess Androgens in PCOS [95]

9.Management and Treatment

A.Lifestyle Modifications:

I. Exercise

Adolescent PCOS management increasingly emphasizes the need for lifestyle changes and non-pharmacological therapies. During the COVID-19 pandemic, a study on Iranian schoolgirls looked at the effects of 12 weeks of aerobic exercise on the hormone levels and lipid profiles of girls with polycystic ovarian syndrome (PCOS). After 12 weeks of aerobic exercise, the analysis's results demonstrated that although high-density lipoprotein levels rose, testosterone, prolactin, estrogen, body weight, BMI, cholesterol, triglycerides, and low-density lipoprotein levels all statistically significantly decreased. The aforementioned research indicates that aerobic exercise is a non-invasive, effective method that should be a significant part of treatment for women with PCOS and improves their health [96]. Exercise is thought to be crucial for human health Exercise is the best medical treatment for all embolic symptoms and is regarded as being just as vital to human health as diet. Since adipose tissue is a major cause of insulin resistance and androgenism, exercise and weight loss are crucial in PCOS [97–98].

II. Obesity

Obesity is commonly seen in people with PCOS, with a prevalence ranging from 33% to 88%. This excess weight can significantly impact fertility and result in a number of reproductive complications, such as irregular menstruation, anovulation, reduced miscarriage rates and fertility. For this reason, controlling weight in the early stages of PCOS is essential to enhance fertility and general quality of life. Abdominal obesity in women with PCOS throughout childhood, maturity, and menopause is primarily caused by hyperandrogenism, which is defined by increased levels of androgens (male hormones) [99].

III.Diet

Controlling carbohydrate intake and adhering to a low glycaemic index (GI) diet are crucial dietary recommendations for PCOS patients. This is particularly crucial because women with PCOS frequently

experience obesity. Lowering energy intake can result in weight loss, which can then affect the regulation of the menstrual cycle, restore ovulation, lower chronic inflammation, improve cardiovascular system, and reduce the risk of cancer [100].

B. Pharmacological Treatment:

Several studies have been conducted on the effects of the combination oral contraceptive (OC) drug, pioglitazone-metformin flutamide (PioFluMet) and spironolactone-pioglitazone-metformin (SPIOMET). A study published in Endocrinology Frontiers examined the effect of treating non-obese teenage girls with PCOS on Folli statin levels, claiming that high Folli statin levels are associated with an increased risk of type 2 diabetes and PCOS. It has been demonstrated that while Folli statin concentrations increase with OC therapy, they remain stable when PioFluMet or SPIOMET is combined. After six months of OC use, Folli statin levels increase significantly. Additionally, Folli statin showed a favourable correlation with changes in both liver fat content and mean serum insulin levels during the OGTT in the sample of women with PCOS under study [101]. Another study looked at thyroid stimulating hormone (TSH) levels in adolescent PCOS patients, as well as how low-dose SPIOMET and OC treatment affected TSH levels. This showed that PCOS patients had higher average levels of TSH compared to girls in the control group. Furthermore, TSH levels fluctuated between OC and SPIOMET treatment, remaining higher with OC and falling rapidly w levels of serum insulin during the OGTT in the SPIOMET. Both subgroups had stable TSH levels after treatment. TSH levels during therapy were correlated with changes in liver fat, but not with changes in total body weight or circulating androgens. How PCOS therapy affects androgen levels has also been researched. Both testosterone and 11-ketotestosterone (11-KT) were lower in those receiving COCP treatment than in those receiving other forms of birth control. those with PCOS who were not treated. Testosterone levels decreased while taking metformin, although 11-oxyandrogens remained unaffected [102]

I. Metformin

Patients with PCOS are treated with metformin for IR. In general, hormonal, metabolic, and reproductive processes improve when IR and excessive androgenization are treated. Metformin works by reducing glucose synthesising the liver, decreasing intestinal absorption, and raising insulin sensitivity. Unwanted side effects include diarrhea, headaches, nausea, vomiting, flatulence, weakness, indigestion, and stomach pain. severe renal failure, acute or chronic metabolic acidosis, including diabetic ketoacidosis with or without coma, and known hypersensitivity to metformin hydrochloride, and other conditions may be contraindications to metformin treatment [103–104–105]. Metformin may delay the onset of PCOS, although it had no effect on fasting glucose, serum lipids, or anthropometric characteristics in women with PCOS. Progression of glucose intolerance. It has also been demonstrated that other insulin-sensitizing drugs work well for treating PCOS [106].

II. Oral contraceptives

OCPs are considered first-line treatment for individuals with PCOS who do not intend to become pregnant. OCPs are not only beneficial in regulating the menstrual cycle, but they also induce testosterone secretion and regulate other physiological functions [107]. There have been reports of OCPs that may significantly reduce the chance of developing endometrial cancer. OCPs are a mixture of progestogen and estrogen, where the estrogen is designed to reduce LH and FSH levels; When LH and FSH levels decrease, T is suppressed and androgen secretion is reduced. For women with PCOS who have low androgenic activity, progestogens are usually recommended [108].

III. Anti-androgens (e.g., spironolactone)

contraceptives are not recommended for women who have ir or metabolic syndrome. using anti-androgens is a much safer option. antiandrogens are known to be a successful therapeutic approach to reduce excess androgens and, consequently, the clinical symptoms associated with high androgen levels. when antiandrogens are taken, ir is reduced [109].

(E.G., SPIRONOLACTONE)

for the treatment of pcos, two types of antiandrogens have been suggested: 5-alpha reductase inhibitors, like finasteride, and androgen receptor antagonists, like flutamide and spironolactone. However, there is a dearth of data regarding the clinical results of antiandrogen combination therapy in adolescents with pcos [109–110]. Spironolactone (aldactone®), an antiandrogen, is used to treat hirsutism and acne. It encourages potassium retention and the excretion of water and sodium because of its competitive antagonistic effect on aldosterone receptors. Gynecomastia is a side effect of this medication; hyperkalemia, Addison's disease, and eplerenone use are contraindications. Because it impacts all facets of the disease's pathophysiology, such as the peripheral conversion of androstenedione to testosterone and its direct action on 17hsd in the ovaries and adrenal glands, which lowers androgen synthesis, spironolactone is a medication for PCOS., and blockade of the androgen receptor. this drug exhibits potent anti-inflammatory and anti-aldosterone properties [111].

C. Surgical Options

I. Ovarian drilling (rarely used)

The first successful laparotomic “wedge resection” operation for the treatment of infertile PCOS women was documented by Stein and Leventhal in 1935 [116]. Despite these encouraging results, the considerable risk of pelvic adhesions after surgery made pharmaceutical treatment superior to surgical strategies. Surgical intervention for CC-resistant PCOS cases significantly improved when laparoscopic ovarian drilling (LOD), a less invasive procedure, was introduced [117]. The basis of this method is to make an arbitrary number of holes in the surface of the ovary. Several Research has revealed a diversity up to 40 pores per ovary. So far, a variety of devices have been employed, including simple incision, bipolar electrocauterization, monopolar diathermy, and several laser systems: Nd: YAG, CO2, or argon [118]. Ovarian drilling may improve the ovarian response to FSH stimulation in IVF cycles, following ovarian drilling and IVF, resulting in a greater quantity of oocytes recovered and a significant increase in embryo growth [119]. However, these findings should be interpreted cautiously because, following ovariectomy and drilling, the authors used noticeably higher FSH dosages in IVF cycles [120].

II.Laparoscopic ovarian drilling risks

Apart from general concerns, the development of de novo adhesions is the primary risk associated with laparoscopic surgery. In a rabbit-based experimental investigation, Keckstein et al [121]. To exhibit high levels of adhesion. Following CO2 laser 3 of 13, Argon laser 1 of 10, and Nd: YAG laser 1 of 19, adhesion rates were unaffected by the type of laser used. During second-look laparoscopy, ovarian adhesions were resolved in eight of eight human patients [122]. Despite the rarity of the usual risks, there has been one documented instance of pelvic infection after LOD [123]. In transvaginal hydrolaparoscopy, Casa et al [124].

D. Psychological Support

1. Decrease in Androgen Manufacturing

Decreased androgen production as excess testosterone and androstenedione are produced by ovarian theca cells in PCOS, a portion of the stromal and androgen-producing theca tissue is destroyed during ovarian drilling. It helps restore follicular maturation, reduces blood androgen levels, and reduces LH secretion (via negative feedback) [125].

2. LH/FSH Ratio Normalization

Follicle selection is hampered in PCOS by high LH and low/normal FSH Following drilling, follicular recruitment and ovulation are improved as FSH slightly increases and LH declines [126].

3. Decrease in Cortical Thickness and Ovarian Stromal Volume

The swollen stroma and thicker cortex of PCOS ovaries mechanically prevent ovulation. Drilling, or making punctures, thins the cortex, which promotes follicular rupture and regular ovulation [127].

4. Anti-Müllerian Hormone (AMH) decline

Small antral follicles produce AMH, which is increased in PCOS and prevents follicular recruitment. Normal folliculogenesis is restored when ovarian drilling lowers AMH [128].

5. Increased Sensitivity to Insulin

The production of androgen by the ovaries is increased by hyperinsulinemia. A slight improvement in insulin sensitivity (lower HOMA-IR) is seen after drilling, which may be due to a decrease in androgens [129].

6. Hypothalamic-Pituitary-Ovarian (HPO) Axis Restitution

Pituitary sensitivity is improved by normalized LH/FSH feedback and decreased androgens.
This results in regular cycles and spontaneous ovulation [130].

Conclusion

PCOS, or one well-known and incredibly complicated endocrine condition is polycystic ovarian syndrome. - metabolic disease that affects women worldwide. This review emphasizes that the fundamental pathophysiology of the condition is based on the ongoing interaction between hyperandrogenism and systemic insulin resistance (IR), which jointly cause specific ovarian dysfunction and place patients at risk of metabolic syndrome and chronic inflammation. Achieving timely and accurate diagnosis is still difficult, mostly because the syndrome is variable and diagnostic criteria are still difficult to apply consistently, especially in adolescents and ethnically diverse groups. Failure to detect PCOS at an early stage increases the lifetime burden of associated co-morbidities, such as type 2 diabetes, cardiovascular disease and gynecological malignancies, and delays essential management. Achieving quick and accurate diagnosis is still challenging, mostly due to the variability of the syndrome and the difficulty of consistently applying diagnostic criteria, especially in adolescents and ethnically diverse populations. Early detection of PCOS reduces the lifetime burden of associated co-morbidities, including cardiovascular disease, gynaecological cancers, and type 2 diabetes, and defers necessary treatment.

Importance of awareness of all diagnosis

Accurate diagnosis and successful treatment of polycystic ovary syndrome (PCOS) depend on complete knowledge of all diagnostic standards, such as the AE-PCOS 2006, Rotterdam 2003, and NIH 1990 definitions. Because PCOS is a heterogeneous disorder, each set of criteria highlights specific features of the condition, such as hyperandrogenism, ovulatory dysfunction, and polycystic ovarian size [136]. Underdiagnosis or overdiagnosis may result in ignoring or irregular application of diagnostic frameworks, postponing treatment and increasing the possibility of long-term problems such as infertility, metabolic syndrome and cardiovascular disease [137]. Therefore, to guarantee thorough assessment, prompt intervention and personalized patient care, physicians and other health personnel must be aware of all diagnostic criteria [138]. Additionally, increased awareness encourages more similar research and better understanding of the prevalence and consequences of PCOS worldwide [139].

Emphasis on early detection and holistic assessment

To avoid long-term reproductive, metabolic, and psychological problems, polycystic ovary syndrome (PCOS) must be identified early and evaluated holistically. Early detection enables hormonal control, metabolic monitoring and lifestyle changes that can enhance fertility and reduce the risk of heart disease, type 2 diabetes, and endometrial disease [140]. More personalized and efficient therapy is made possible by a holistic evaluation method that considers not just reproductive symptoms but also metabolic health, mental health and quality of life [141]. Women with PCOS can achieve comprehensive treatment and long-term health benefits by integrating multidisciplinary management, including gynaecological, endocrine, nutritional, and psychological examination [142–143]. To improve overall outcomes and reduce the lifetime burden of PCOS, it is essential to prioritize early diagnosis and comprehensive screening.

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