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Poly cystic ovary syndrome: A Comprehensive review on Pathophysiology, Management and Emerging insights

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ABSTRACT
Polycystic Ovary Syndrome (PCOS) is a widespread hormonal condition that typically affects individuals with ovaries during their reproductive years. It presents a range ofsymptoms, including disrupted menstrual cycles, heightened levels of male hormones (androgens), and cyst-like structures on the ovaries. These imbalances may lead to various health concerns such as infertility, excess weight gain, skin issues like acne, and unusual excessive hair development on chest and Face . Although the exact origin ofPCOS is not clearly understood, both hereditary and environmental influences appear to play a role. Diagnosis generally involves evaluating the patient's symptoms, performing physical assessments, and using imaging tools like ultrasound. While there is no permanent cure for PCOS, its symptoms can often be controlled through lifestyle interventions—such as a balanced diet and consistent physical activity—and medication to address hormonal irregularities. Detecting the condition early and providing suitable treatment can reduce the riskof long-term health issues such as heart disease and type 2 diabetes, emphasizing the need for greater awareness and ongoing research.

Keywords: Polycystic Ovary Syndrome, (PCOS) Treatment-Seeking Behavior, Hormonal disorder, Biomarkers, infertility

I. INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a frequently occurring hormonal disorder that mainly affects individuals with ovaries during their reproductive years. It is characterized by a group of symptoms such as irregular or absent menstrual periods, an over production of androgens (male hormones), and the presence of multiple cysts on the ovaries. These hormonal disruptions often lead to complications such as infertility, weight gain, acne, and excessive hair growth in areas like the face, chest, and back.

Although the root cause of PCOS remains unclear, experts believe it results from a combination of genetic predispositions and environmental factors. Diagnosis is typically made based on clinical symptoms, hormone testing, and imaging studies, particularly pelvic ultrasound.[1]PCOS is among the most prevalent hormonal disorders affecting women of reproductive age worldwide . First identified by Stein and Leventhal in 1935, PCOS remains a diagnosis of exclusion—meaning that other potential causes of similar symptoms must be ruled out before confirming it. Delayed identification of the condition can worsen its effects, making it harder to manage and increasing the risk of developing other health issues.

PCOS is linked to several other health conditions, including infertility, obesity, insulin resistance, type 2 diabetes, metabolic syndrome, cardiovascular risks, depression, sleep disturbances, and an increased risk of endometrial cancer. Timely diagnosis and lifestyle interventions are key to improving quality of life and long-term outcomes.

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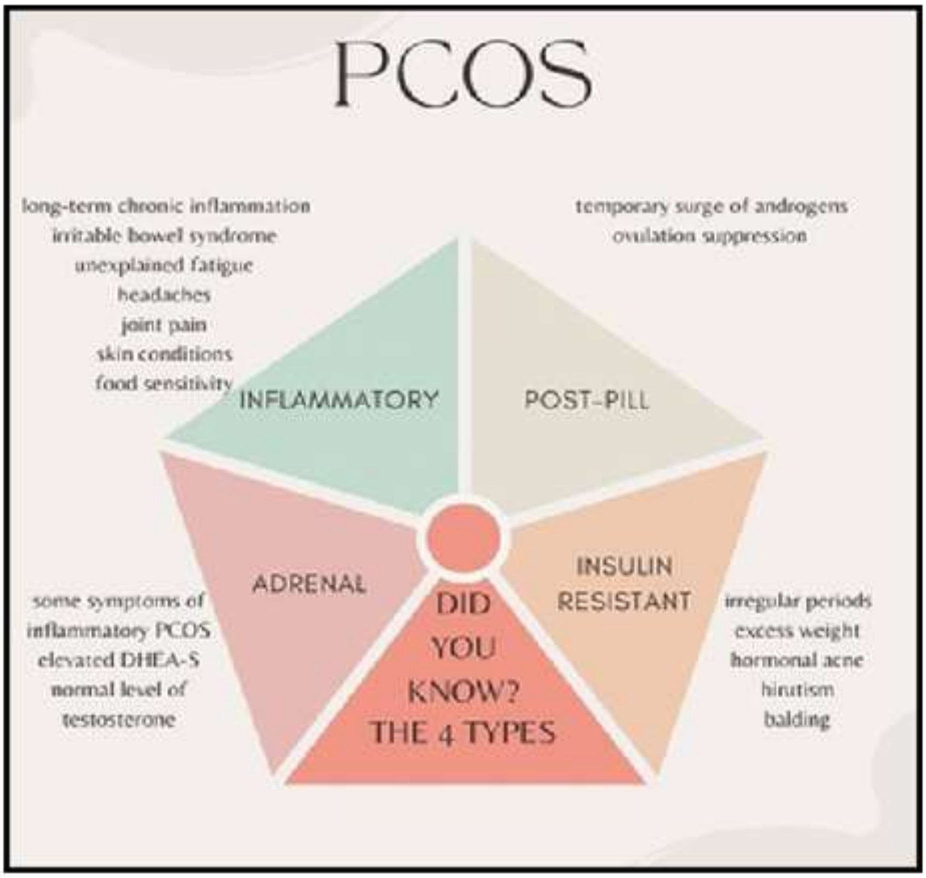

Fig1:Depicts the major types and causes of polycystic Ovary Syndrome along with symptoms

Factors responsible for polycystic ovary syndrome

Polycystic Ovary Syndrome (PCOS) is a complex hormonal disorder influenced by a combination of genetic, lifestyle, and environmental factors. Here are the main factors responsible for PCOS:

Genetic Predisposition: PCOS often runs in families, indicating a possible genetic link. Specific gene variations may affect hormone regulation and insulin sensitivity, increasing the likelihood of developing the syndrome.

Excess Androgens: increased levels of male chemicals, such as testosterone, disturb the normal functioning of the ovaries, leading to irregular ovulation or its complete absence.

Imbalanced LH and FSH: A higher percent of luteinizing hormone (LH) to follicle-stimulating hormone (FSH) can interfere with the ovulation process.

Insulin Resistance: The condition affects how the body processes insulin, often resulting in increased insulin levels. This increase can Activate the ovaries to produce More androgens, further disturbing hormonal balance.

Inflammation and Obesity: Low-grade chronic inflammation and being overweight or obese are also known to play a role in the onset and severity of PCOS. These factors not only affect insulin function but also exacerbate hormonal deregulations. Other several factor such as inflammation obesity environmental factors lifestyle related factors are responsible for the PCOS. [3]

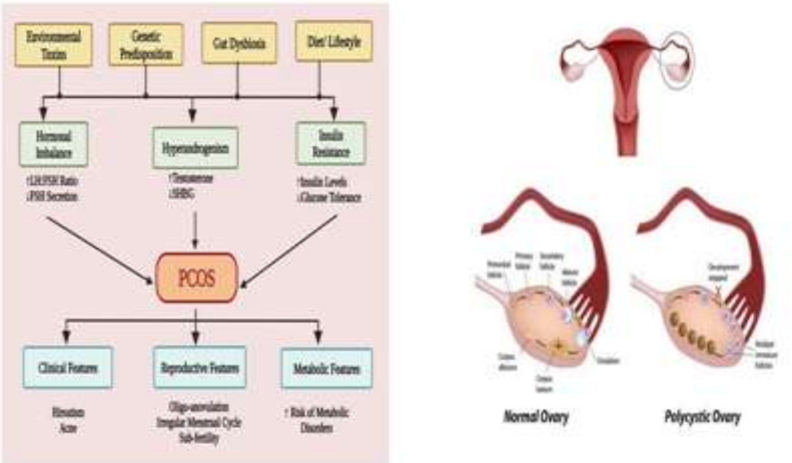

Fig 2:How factors responsible for the Polycystic Ovary Syndrome &lit's clinicalapproaches

Etiology of polycystic ovary syndrome

The exact origin of PCOS is still under investigation, but several interconnected biological processes are believed to play significant roles. One of the core issues identified in many individuals with PCOS is insulin resistance, which can occur even in those who are not overweight. Elevated insulin levels—referred to as hyperinsulinemia—Activate the ovaries to produce more male hormones, disrupting the hormonal balance.

This rise in androgens decreased levels of sex hormone-binding globulin (SHBG), a protein that normally binds excess testosterone, resulting in higher concentrations of free testosterone in the body. These hormonal disruptions lead to abnormal development of the ovarian follicles, contributing to infertility and visible changes in ovarian structure.

Obesity tends to amplify insulin resistance, creating a cycle where hormonal imbalances become more pronounced. As a result, weight gain and metabolic dysfunction often make PCOS symptoms worse. However, studies have shown that even modest lifestyle changes—like engaging in regular physical activity and adopting a healthier diet—can significantly reduce insulin resistance and improve overall hormonal balance.[4]

Research has also found that insulin can directly affect the ovarian theca cells, leading to increased an drogen production, independent of body weight. Despite the strong association, insulin resistance is not observed in every individual with PCOS, indicating that the syndrome's causes are complex and multi factorial.

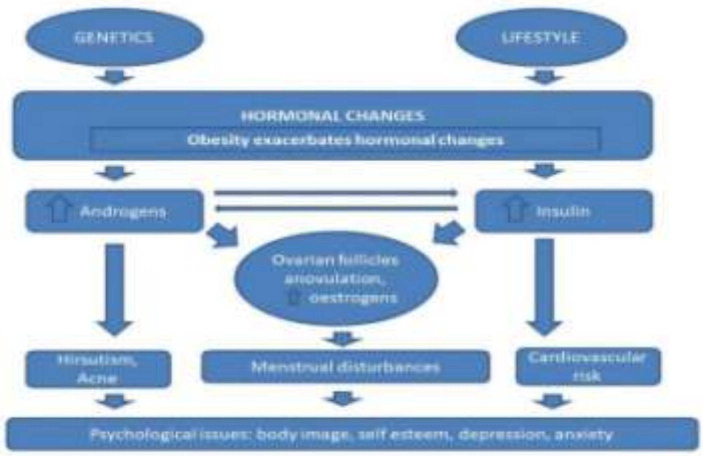

Fig3: Etiology of polycystic ovaries syndrome

Pathophysiology of polycystic ovary syndrome

The underlying mechanisms of PCOS primarily involve hormonal dysfunction, particularly an excess production of androgens and disrupted ovarian function. In most individuals with PCOS, the ovaries exhibit heightened sensitivity to gonadotropin stimulation, leading to an overproduction of androgens such as testosterone. This over activity is often reflected in an exaggerated response of 17-hydroxyprogesterone (17-OHP) to hormonal Activation which is a marker of ovarian androgen excess. Approximately two-thirds of PCOS cases display this pattern of functional ovarian hyper androgenism, while a smaller group shows signs of adrenal involvement in androgen overproduction. Though specialized testing for adrenal androgen excess exists, it is not commonly used in clinical settings due to limited diagnostic value. [5]

The hormonal imbalance caused by high levels of androgens affects the development and progression of ovarian follicles. It accelerates the activation of immature follicles while hindering the selection of a dominant follicle, progress to anovulation and the characteristic polycystic ovarian morphology (PCOM). Luteinizing hormone (LH) often appears in elevated levels in individuals with PCOS. While LH supports the production of sex steroids, persistent LH elevation can lead to the desensitization of ovarian cells, further aggravating the hormonal imbalance. The imbalance between LH and follicle-stimulating hormone (FSH) also contributes to inadequate change of androgens to estrogens in the ovaries due to reduced aromatase activity in granulosa cells.[6]

In individuals with higher body fat, especially in adipose tissue, there is an elevated peripheral change of androgens to estrogens, primarily estrone. This abnormal estrogen production feeds back to the hypothalamus and pituitary gland, preventing the natural cyclic hormonal variations necessary for normal menstrual cycles and ovulation. The result is often endometrial hyperplasia, due to prolonged unopposed estrogen stimulation. Emerging research also indicates a potential role for chronic low-grade inflammation and autoimmune pathways in disrupting normal follicular development, which may further impair fertility in women with PCOS.

Causes of polycystic ovary syndrome

The precise cause of PCOS is not fully understood, but it is widely accepted that several interacting factors contribute to its development. These include genetic, hormonal, and metabolic influences, with obesity and insulin resistance acting as major contributors.[7]

Androgen Excess: Increased levels of androgens, or male hormones, disturbance with the normal release of eggs during ovulation. This chemical imbalance can result in uneven or absent menstrual cycles, as well as the development of small fluid-filled follicles on the ovaries. High androgen levels are also responsible for symptoms

Genetic Influence: Family history appears to increase the likelihood of developing PCOS, indicating that inherited genes may play a significant role.

Chronic Inflammation: Low-level inflammation is commonly observed in people with PCOS. Blood tests may reveal elevated markers such as C-reactive protein (CRP) and white blood cell counts, indicating ongoing inflammation. This persistent inflammatory state may also contribute to the hormonal imbalances seen in PCOS.[8]

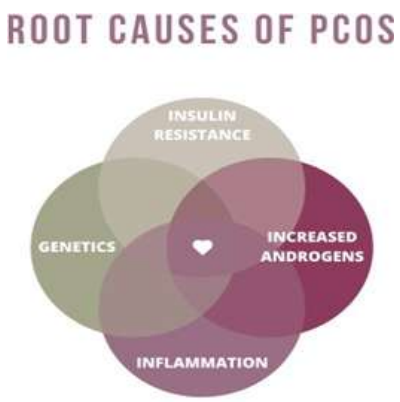

Fig 4: Root cause of PCOS

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Symptom of polycystic ovary syndrome

Irregular Menstrual Cycles: This may involve infrequent, absent, or very heavy periods. Some individuals might miss their periods for several months, while others experience excessive bleeding.

Excessive Hair Growth (Hirsutism): Up to 70% of individuals with PCOS may notice abnormal hair growth on the face, chest, back, or abdomen due to increased androgen levels.[10]

Acne and Oily Skin: Hormonalim balances can lead to persistent acne, particularly on the face, chest, and back, which may be resistant to typical skin treatments. obesity, cysts, skin tags, infertility are other some symptoms of Polycystic Ovary Syndrome[11]

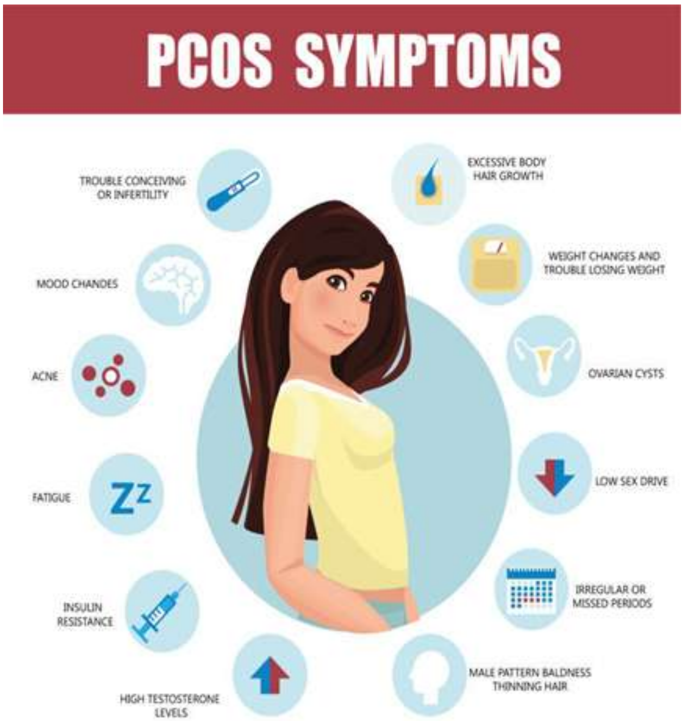

Fig5: Symptoms of polycystic ovary syndrome

Diagnosis and treatment of Polycystic ovary syndrome

PCOS cannot be diagnosed with a single test. Instead, doctors usually use a combination of medical history, physical exams, laboratory tests, and imaging techniques to make an accurate diagnosis. The evaluation process often involves the following steps:

Clinical Evaluation: The doctor will begin by discussing your symptoms, menstrual patterns, weight changes, and any history of excess hair growth or acne. A physical exam may include measuring body mass index (BMI) and checking for visible signs of hormonal imbalances..

Pelvic Examination: This allows the healthcare provider to detect any abnormalities in the reproductive organs, such as enlarged ovaries or other structural changes.

Hormonal Blood Tests: Blood samples are used to evaluate levels of key hormones, including testosterone, LH (luteinizing hormone), FSH (follicle-stimulating hormone), and thyroid hormones. These tests also help rule out other conditions with similar symptoms.

Glucose and Lipid Testing: Tests may also assess insulin levels, blood sugar regulation (glucose to lerance), and lipid profile to evaluate metabolic health. Ultrasound Imaging: A transvaginal ultrasound provides detailed images of the ovaries and uterine lining. It helps detect the presence of many small follicles—an indicator of polycystic ovaries.[12]

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Symptoms	Treatment
Obesity, weight gain	Weight loss options include: • changes to diet • exercise • medications, i.e. orlistat (Xenical®) • surgery, i.e. gastric bypass, lap-band
Hirsutism (hairiness)	• medications, i.e. insulin lowering agents, such as metformin, oral contraceptive pill, anti-androgens • cosmetic treatments, i.e. waxing, bleaching, laser, electrolysis • weight loss
Acne	• topical creams • medications, i.e. oral contraceptive pill, insulin lowering agents, such as metformin, anti-androgens
Insulin resistance Diabetes	• weight loss • changes to diet • exercise • medications, i.e. insulin lowering agents, such as metformin
Infertility caused by irregular periods and ovulation	• weight loss • medications, i.e. clomiphene citrate (Serophene®, Clomid®), insulin lowering agents, such as metformin, oral contraceptive pill –see page 16

Fig 5: symptom and treatment of polycystic ovary syndrome

Treatment strategies: Insulin resistance

Insulin resistance is a central feature of PCOS in many individuals and plays a major role in the development of symptoms such as irregular periods, infertility, and excess androgen production. Managing insulin resistance is, therefore, a crucial component of PCOS treatment. Metformin, a medication primarily used to treat type 2 diabetes, is one of the most commonly prescribed drugs for addressing insulin resistance in PCOS. It works by:

Enhancing the body's sensitivity to insulin, Reducing insulin levels in the bloodstream, Helping to lower androgen production by the ovaries, In addition to improving insulin metabolism, metformin may also support: Weight management, Regulation of menstrual cycles, Restoration of ovulation in some individuals.[13]Metformin is often used in combination with other therapies, such as clomiphene citrate, to boost ovulation, particularly in individuals who are resistant to clomiphene alone.[14]Although not officially approved for PCOS treatment in adolescents ("off-label" use), metformin is widely used in teenagers showing clear signs of PCOS or insulin resistance. Clinical guidelines suggest it can be considered as an add-on to lifestyle changes when symptoms are pronounced or diagnosis is certain.

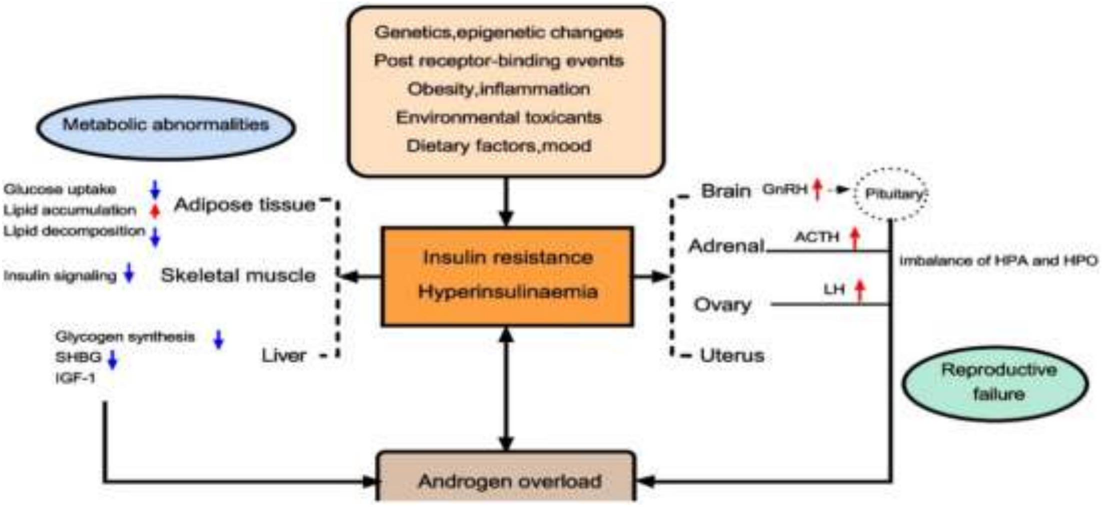

Fig6: insulin resistance the rapies in Polycystic Ovary Syndrome

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Treatment strategies: improvement of fertility

Infertility is one of the most common concerns for individuals with PCOS, primarily due to irregular or absent ovulation (an ovulation). However, fertility can often be improved through targeted interventions, starting with lifestyle changes and followed by medical treatments if needed. The first line of treatment for improving fertility in PCOS often involves changes in diet, physical activity, and weight management. Even modest weight loss—as little as 5–10% of total body weight—can: Restore regular ovulation Improve menstrual cycle patterns Increase the chances of natural conception Research has shown that lifestyle changes can lead to significant improvements in reproductive function, particularly in individuals with overweight or obesity. Ovulation induction medications typically produce results within 3–6menstrualcycles. If pregnancy is not achieved after several cycles of ovulation, alternative or more advanced treatments— such as gonadotropin therapy or assisted reproductive technologies (ART)—may be considered. Close monitoring through ultrasound and hormone level testing is crucial to reduce risks, such as ovarian hyper stimulation or multiple pregnancies.[15]

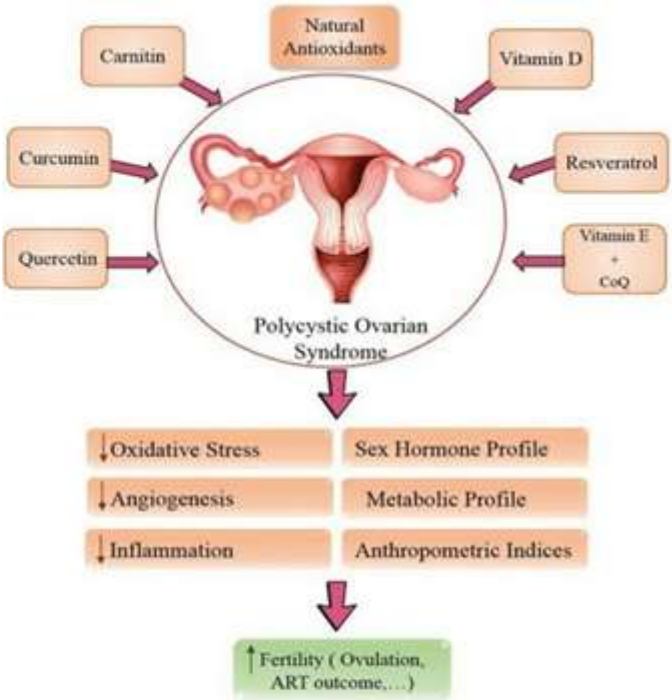

Fig7: Improvement of Fertility in Polycystic Ovary Syndrome

Hormonal therapies: oral contraceptives

Hormonal therapies play a central role in managing several symptoms of PCOS, particularly those related to menstrual irregularity, acne, and excessive hair growth. These therapies are also used in treating fertility challenges by inducing ovulation when natural hormonal signals are not functioning properly.

Clomiphen Citrate

When the goal is to become pregnant, clomiphene citrate is often used to initiate ovulation. It functions by prompting the hypothalamus so release gonadotropin-releasing hormone (GnRH), which then signals the pituitary gland to increase production of FSH and LH. These hormones are essential for the development and release of mature eggs Clomiphene is generally effective in individuals who are a novulatory but have functional ovaries. Most patients who respond to clomiphene will ovulate and conceive within 3 to 6 cycles. If ovulation occurs but pregnancy does not follow, or if ovulation does not happen at all, further treatment options such as gonadotropins may be considered.[16] Clomiphene is often used as a first-line fertility medication in PCOS and has a long history of safety and effectiveness. However, if it fails to produce the desired results after a few

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cycles, healthcare providers typically reassess the treatment plan. [17]Oral contraceptive pills (OCPs), which contain synthetic forms of estrogen and progesterone, are frequently prescribed for individuals not seeking pregnancy.

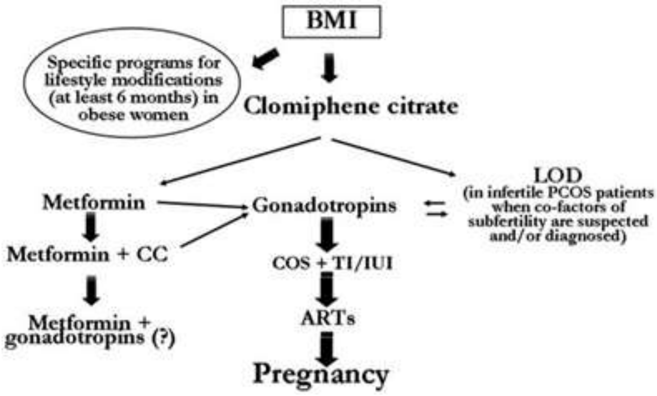

Fig 8: Hormonal therapies for oral contraceptives (clomiphene citrate) methodology

Gonadotrophins

When oral medications like clomiphene citrate are ineffective in inducing ovulation, gonadotropin therapy may be recommended as a second-line treatment. Gonadotropins are injectable medication (chemical) that directly Activate the ovaries to Make and mature multiple follicles, increasing the chances of ovulation and conception.

Mechanism of Action: Gonadotropins are synthetic versions ofthe natural reproductive hormones: Follicle-Stimulating Hormone (FSH): Encourages the growth and development of ovarian follicles that contain eggs. Luteinizing Hormone (LH) or Human Chorionic Gonadotropin (hCG): Supports final maturation and the release (ovulation) ofa mature eggs. These hormones are administered through injections, and their effects are closely monitored through ultrasound imaging and blood hormone levels to ensure proper follicular development and reduce risks like ovarian hyperstimulation or multiple pregnancies

Common Medications: FSH Preparations: Medications such as Gonal-f and Follistim provide pure FSH to stimulate follicle growth. Combined FSH/LH: Products like Pergoveris offer both hormones to support more complex cases. hCG Injections: Used to trigger ovulation once follicles are adequately developed (e.g., Ovidrel, Pregnyl). The goal of gonadotropin therapy is to achieve the development of one or two dominant follicles. Excessive follicle growth increases the likelihood of multi plebirths, which is why treatment must be precisely managed. [18] [19]

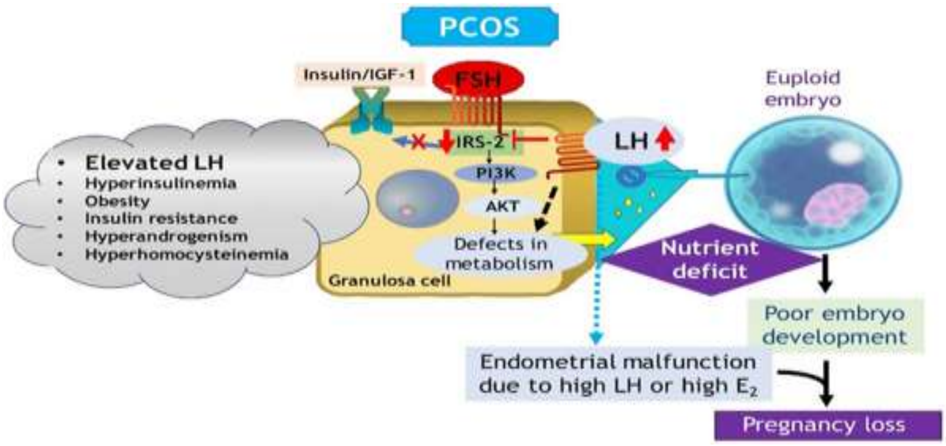

Fig 9: Hormonal therapies for oral contraceptives (Gonadotrophin) methodology

II. CONCLUSION:

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder affecting women of reproductive age characterized by hormonal imbalances, irregular menstrual cycles, and polycystic ovaries. This study explored the various dimensions of PCOS, beginning with its definition and clinical features. The etiology of PCOS is multifactorial, involving genetic, environmental, and lifestyle factors that disrupt normal hormonal regulation Pathophysio logically, insulin resistance hyperandrogenism, and ovariandys function are central contributors to the development and progression of the syndrome. Treatment options for PCOS are diverse and tailored according to symptoms ranging from lifestyle modifications and pharmacologic therapies (such as hormonal contraceptives and insulin sensitizers) to fertility treatments. Proper care and management require a multidisciplinary approach involving regular monitoring, dietary guidance, psychological support, and patient education . Recent research has focused on understanding the molecular mechanisms behind PCOS, identifying potential biomarkers for early diagnosis, and exploring novel treatment options including nutraceuticals, gut microbiome interventions, and gene therapy. While there is still no definitive cure, advancements in research continue to improve the quality oflife and reproductive health outcomes for women reproductive health outcomes for women.

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