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Polycystic ovarian syndrome: An ongoing public health concern

Arpan Dutta[1] , Rumpa Banerjee[2*] , Ankita Banik[2] , Mrityunjay Banerjee[3] , Sourav Chatterjee[4] , Priyankar Chakraborty[2] , Aninda Dutta[2] , Abhijit G. Banerjee[5]

Affiliations:

1. Guru Nanak Institute of Pharmaceutical Science & Technology, Kolkata, India.

2. Eminent College of Pharmaceutical Technology, Barasat, Kolkata, India.

3. Institute of Pharmacy and technology, Salipur, Odisha, India.

4. M.R. Institute of Pharmaceutical Sciences and Research, Bira, WB, India.

5. Genomic Bio-Medicine Research & Incubation., Durg, Chattisgarh, 491001, India.

***Corresponding Authors:**

Rumpa Banerjee: rumpabanerjee1972@gmail.com

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KEYWORDS

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ABSTRACT

Polycystic ovarian syndrome (PCOS) is a condition of the endocrine system that is extremely ubiquitous among women in the reproductive phase. Ovarian dysfunction, hormonal disruptions, and metabolic abnormalities are the main characteristics of this disease. PCOS affects approximately 5-10% of female candidates who are of childbearing age. Many researchers have spent many years trying to uncover the root of this illness but to no avail. The underlying origin of this varied illness, which is often associated with obesity, is unknown. PCOS is usually diagnosed when exploring hirsutism or amenorrhea/oligomenorrhea, but the severity and clinical symptoms of PCOS vary greatly across individuals. PCOS is reportedly one of the causes of infertility. Technically, there is no recognized definition for PCOS; nonetheless, it has been argued that among the following three features, two are necessary for diagnosis: irregular menstruation; a biochemical or clinical androgen excess as depicted through laboratory tests; and the presence of multiple ovarian cysts. Females suffering from this condition are more likely to have emerging glucose intolerance; hence, some experts endorse screening for cardiovascular risk factors and type 2 diabetes, which are directly associated with metabolic syndrome. Infertility, irregular uterine bleeding, gestational diabetes mellitus, anxiety and pregnancy-induced hypertension are all possible complications of pregnancy. Thiazolidinediones are effective at treating PCOS by increasing insulin sensitivity and normalizing irregular menstruation; however, they should be avoided by women who are trying to conceive. In addition, increasing hormone levels and stimulating ovulation may be aided by a balanced diet that features a longer breakfast and a shorter dinner. This post will provide a concise overview of polycystic ovary syndrome.

Introduction:

Abnormal, closed sac-like structures known as cysts are found within several types of tissue and may contain fluid, gas, or semisolid material [1]. Cysts can form at various sizes and locations on the body. The cyst's exterior layer, known as the capsular layer, is what is meant by the term "cyst wall." The presence of many cysts in an ovary is what is meant by the term "polycystic ovary" [2,3]. Although Stein and Leventhal often reported the presence of polycystic ovarian syndrome [4], in 1721, an Italian physician named Vallisneri reported a case of infertility in a married woman with pigeon egg-sized ovaries due to polycystic ovarian disease. In the early 1990s, during an NIH-sponsored symposium on polycystic ovary syndrome (PCOS), formal diagnostic criteria were established and thereafter widely adopted. Many studies have investigated the pathogenesis of PCOS. Many of us occasionally misunderstand tumors with cysts, believing that a cyst is a tumor that later exhibits malignant activity.

Women worry because they believe that having a cyst before becoming pregnant will prevent them from experiencing pregnancy; however, this is a completely false belief. A woman can prevent infertility that PCOS typically causes if she receives an early diagnosis [5]. Observing some people in this day and age leading superstitious lives is extremely upsetting. Some of their terminology includes the idea of a "curse," which they use to refer to a woman who has polycystic ovaries and who, if discovered to be infertile, is subjected to indirect or even direct physical harassment as well as mental anguish. Witnessing some people in the twenty-first century leading superstitious lives is extremely upsetting. Some of their terminology includes the idea of a "curse," which refers to a woman who has polycystic ovaries and who, if discovered to be infertile, is subjected to indirect or even direct physical and psychological abuse. This is unquestionably a result of inadequate education. Compared to a typical woman, a woman with PCOS has the same potential to expect a successful pregnancy. PCOS is now widely recognized among women and is highly common. Therefore, a woman's most crucial responsibility is to see a gynecologist as soon as she experiences any problems, particularly if those concerns are monthly.

Description:

The female pelvic reproductive organs, known as the ovaries, are in charge of producing sex hormones in addition to housing the ova. The organs in the wide ligament beneath the uterine tubes are paired on either side of the uterus. The ovaries are positioned in the ovarian fossa, which is bordered by the ureter, the removed umbilical artery, and the external iliac arteries. A female can ingest between 200 and 300 million eggs at birth, but only 300 will develop and be unconfined for fertilization [6].

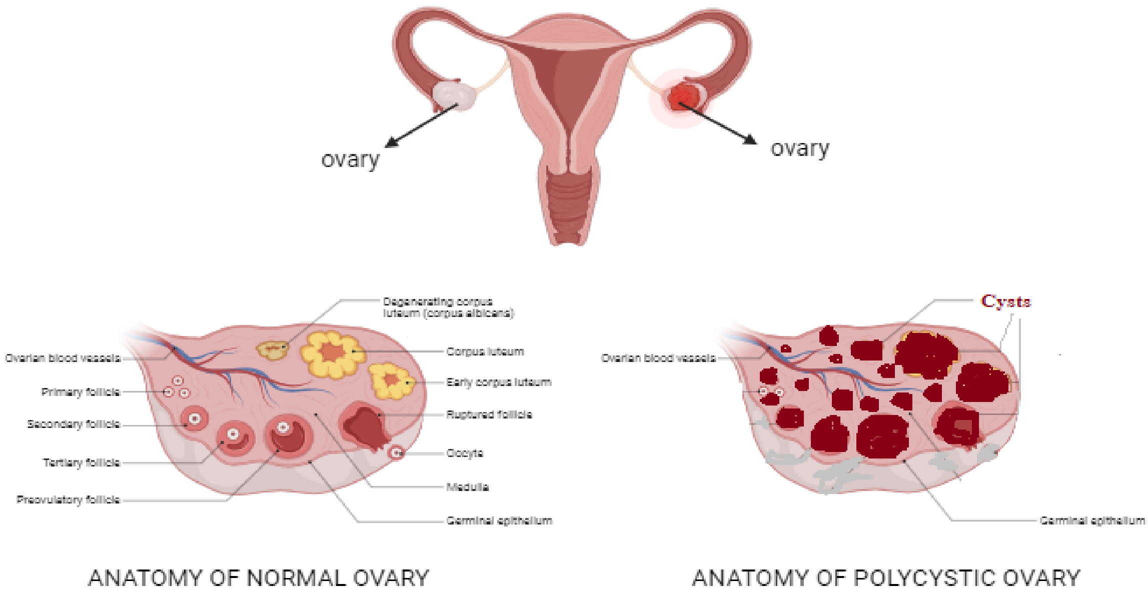

Fig 1: Diagram showing a comparison between the structure of a normal ovary and a polycystic ovary created by biorender.com software

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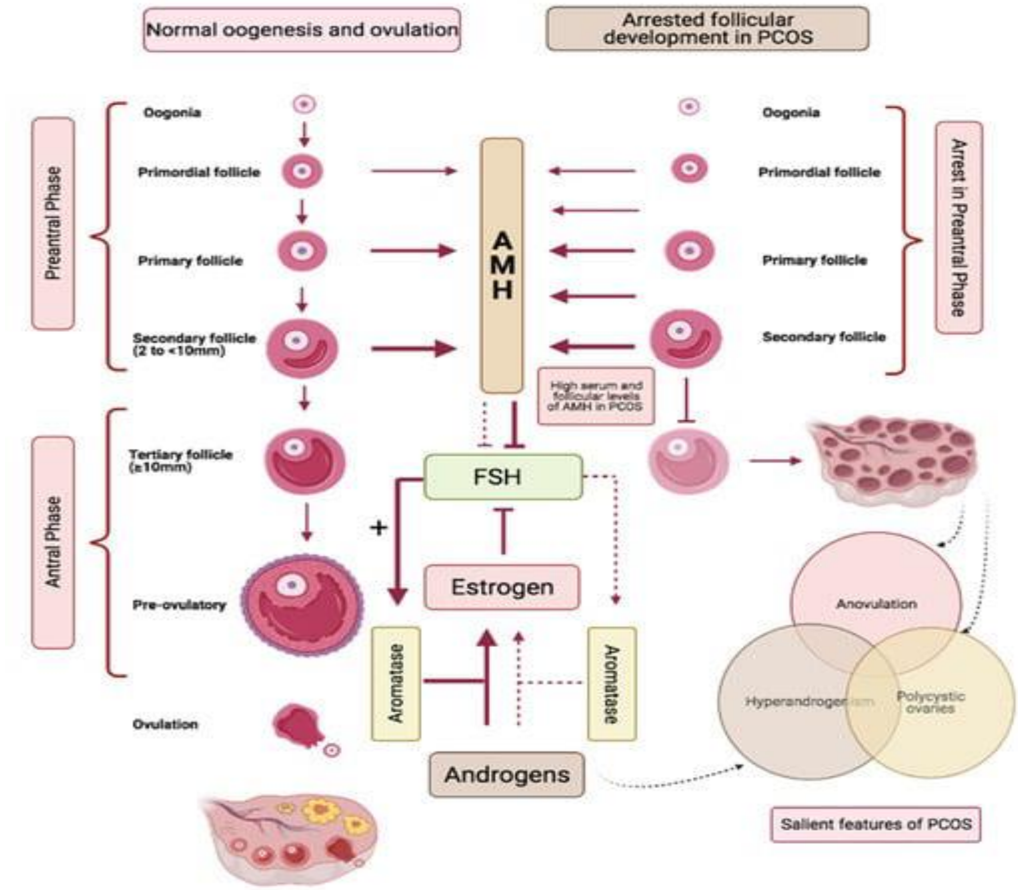
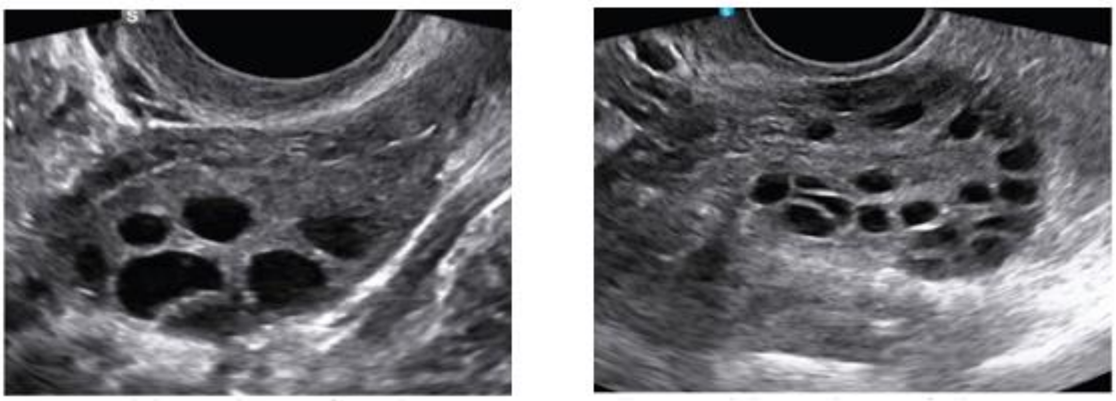


Fig 2: Graphical abstract of a comparison study of changes in normal ovaries and polycystic ovaries during folliculogenesis [7].

According to the researchers, polycystic ovaries are characterized by either an ovary with 12 or more follicles in a single plane, each measuring between 2 and 10 millimeters in size [8], or an ovary with a volume greater than 10 mL but no dominating follicle [9]. Transvaginal ultrasonography can be used to compare the differences between two ovaries to acquire a clearer understanding [10].



a) Transvaginal ultrasound image of normal Ovary **b) Transvaginal ultrsound image of Polycystic Ovary**

Fig. 3 : Differences between polycystic and normal ovaries according to transvaginal ultrasound; a) normal ovary showing few follicles of varying sizes; b) polycystic ovary showing many follicles of nearly similar sizes (approx. 2-5 mm) [11].

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Etiology:
According to Umland EM *et al*., polycystic ovary syndrome (PCOS) is an oligogenic illness in which several environmental and genetic variables interact to yield an individual's unique biochemical and clinical phenotype. Even though the exact genetic cause of PCOS is still unknown, it has been observed that this condition tends to persist in families [12]. However, whether PCOS occurs in families has not been definitively established [13]. A poor diet and lack of exercise might amplify environmental factors, including obesity, which has been linked to polycystic ovary syndrome [14,15]. Lifestyle changes, including loss of body weight and exercise, can sometimes reverse PCOS, which can affect propagative and metabolic aspects [16,17]

Pathophysiology:
Many hypotheses have been proposed to date to describe the underlying pathophysiology of polycystic ovary syndrome (PCOS). Initially, it was believed that high levels of androgen produced inside the uterus were primarily responsible for this condition [18].

The occurrence of PCOS in teenage females or an increase in androgen levels in the cord blood of female newborns born to mothers with PCOS has not been linked to recent human research. According to the adipose tissue expandability theory [19], newborns with intrauterine growth restriction (IUGR) and subsequent impulsive catch-up development may have impaired expandability of tissue, resulting in an impaired capacity to store lipids in their fat tissues. Therefore, insulin resistance and hyperandrogenism may be linked [20,21]. However, the pathophysiology of PCOS includes uncontrolled ovarian steroid synthesis, high levels of environmental and oxidative stress, and genetic variables [22].

An underlying defect in theca cells has been linked to hyperandrogenism in females with PCOS [23]. Despite the lack of trophic stimuli, women with PCOS have theca cells that release large amounts of androgens [24]. Patients with polycystic ovary syndrome (PCOS) secrete up to four times more anti-Mullerian hormone than normal controls [25], suggesting that this intrinsic dysregulation also affects granulosa cells. In those with PCOS, an abnormality in apoptotic pathways causes an abnormally high number of mature follicles to develop. The polymorphic marker D19S884 has also been found in the fibrillin 3 gene of separate groups of families with PCOS [26].

Genetics:
From a hereditary perspective, the large association dataset of meta-analyses on three main factors related to PCOS, ovulatory dysfunction (OD), polycystic ovarian morphology (PCOM) and hyperandrogenism (HA), revealed a significant link between PCOS susceptibility variations and PCOS susceptibility. This finding supports the notion that many differences can lead to PCOS through various processes [27].

Epigenetic contributions to PCOS:
Epigenetics is the study of how environmental cues, as opposed to variations in the DNA sequence, can have a lasting impact on gene expression. Increasing evidence suggests that epigenetic changes play a key role in the development and expression of PCOS [28], but the exact origin of PCOS has not been determined. Epigenetic investigations, including noncoding RNA profiling, DNA methylation, and histone modification studies, have been performed on PCOS patient samples and animal models. Recent results on epigenetic changes associated with polycystic ovary syndrome are outlined in this article.

Epigenetic Mechanisms: Epigenetic mechanisms include DNA methylation, chromatin changes, and noncoding RNAs. Alterations in chromatin shape and accessibility of the transcriptional machinery can result in changes in gene expression. Diet, lifestyle, and toxin exposure are just a few examples of the many environmental factors that might affect epigenetic changes. [29]

DNA Methylation: Research has shown that PCOS individuals have different patterns of DNA methylation, which may play a major role in the expansion of this disorder. Gene silencing occurs through DNA methylation, in which a methyl group is added to cytosine residues in CpG dinucleotides. DNA methylation abnormalities have been found in many PCOS-related genes, as well as those implicated in insulin signaling, steroidogenesis, and folliculogenesis [30].

Histone modifications: Histone alterations control chromatin shape and gene expression. Common histone modifications include acetylation, methylation, and phosphorylation. In PCOS, critical genes involved in

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ovarian function, insulin signaling, and inflammation are dysregulated due to changes in histone modifications. Insulin resistance is a common symptom of polycystic ovary syndrome (PCOS) and has been linked to changes in histone acetylation patterns.

Noncoding RNAs: MicroRNAs (miRNAs) and long noncoding RNAs (lncRNAs) are two examples of noncoding RNAs that play important roles in gene regulation. Patients suffering from PCOS have been found to have aberrant expression of miRNAs, which play a vital role in the dysregulation of critical genes associated with ovarian folliculogenesis, steroidogenesis, and insulin signaling. Insulin resistance, inflammation, and androgen excess are linked to polycystic ovary syndrome (PCOS), and lncRNAs have emerged as potential regulators of these pathways.

Environmental Factors: Epigenetic alterations, which may contribute to PCOS formation and progression, are susceptible to environmental influences. Studies have connected altered epigenetic marks in PCOS to parameters such as prenatal revelation to androgens, maternal obesity, and exposure to endocrine-disrupting chemicals (EDCs). Epigenetic alterations in genes involved in ovarian development and metabolic pathways can be induced by environmental factors, increasing susceptibility to polycystic ovary syndrome (PCOS) [31].

Statistics:

In 2012, PCOS was estimated to impact 116 million women (3.4% of the total female population) worldwide, according to the World Health Organization (WHO). PCOS affects anywhere from 2.2% to as high as 26% and 36% of women in India [32]; however, the estimates vary greatly.

Symptoms:

Studying typical symptoms and indicators is the first step in comprehending PCOS [33]. Hence, some of the most prevalent symptoms and indicators for determining whether PCOS may be the cause of our health problems are as follows:

1. Unpredictable periods (oligomenorrhea): This indicates that the cycle length is longer than 35 days rather than just being two or three days late, occasionally. A typical cycle can last anywhere from 22 to 35 days. Due to a shortage of progesterone, PCOS patients have eight or fewer cycles each year [34].
2. Excess hair growth in unexpected places on the body (Hirsutism): Women who have PCOS typically suffer excessive hair development on their face, thumbs, chest, arms, toes, belly, and back since it is a hormonal illness characterized by high quantities of androgens [35].
3. PCOS may lead to overweight or obesity; women with PCOS can afflict slender individuals as well as those who gain weight or are obese, which affects half of all women with PCOS [36].
4. Excess androgen may increase the susceptibility of certain skin types to acne; moreover, increased androgen levels can cause skin issues such as acne [37].
5. Scalp Hair Loss: Women who have an overdose of androgens may also experience hair loss, which manifests as diminishing hair in the head or hair recession, which may be more severe [38].
6. Mood Disorders: A percentage of PCOS-afflicted women experience mental issues. These include eating disorders, anxiety, depressive disorders and poor body image [39,40].
7. Sleep trouble and fatigue: Sleep apnea, characterized by brief pauses while breathing that can cause daytime sleepiness, is most common in females with PCOS. Insomnia and sleep disorders can aggravate mood issues.
8. Difficulty in conceiving: PCOS is the most common cause of female poverty. Lack of ovulation is the cause of fertility issues; therefore, even if a woman is experiencing pregnancy, this does not mean that she is ovulating. Therefore, a woman might not suspect anything amiss until she has been trying to conceive for a while [41].
9. Signs of Insulin Resistance: Type 2 Diabetes is the major aspect of PCOS. Insulin confrontation may develop in women with PCOS because they are less receptive to the hormone insulin, which carries glucose to our cells for energy. In actuality, 65-70% of PCOS-afflicted women have insulin resistance. Women who have insulin resistance may experience skin problems such as skin tags or a condition known as acanthosis nigricans, which causes dark, velvety patches of skin to form around the armpits, groin, and neck [42].

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Diagnosis:
There is no specific diagnostic procedure for identifying PCOS. One must begin by going over their medical history, determining their menstrual cycle frequency, keeping track of weight changes, and having a physical checkup done, which includes looking for any symptoms [43]. A pelvic examination will next be performed to properly check the reproductive organs for masses, growth, or other irregularities [44]. According to some blood tests, DHEAS (dehydroepiandrosterone sulfate) and SHBG (sex hormone binding globulin) may be present [45]. Additional tests were performed to assess triglyceride, cholesterol, and fasting glucose levels. Additionally, transvaginal ultrasounds are carried out to carefully examine the condition of the uterus and ovaries [46,47].

Insulin resistance, body fat distribution, and the emergence of PCOS:
To fully grasp the mechanism behind PCOS development, an in-depth description of the link between fat distribution and insulin resistance is needed. When the body's supply of subcutaneous fat is low, fat is deposited in the liver and other abdominal organs called visceral fat. Blood triglyceride and free fatty acid levels increase, leading to this condition [48]. People with PCOS are at increased risk for developing metabolic syndrome characteristics such as increased waist circumference, obesity, visceral fat, insulin resistance, and hyperinsulinemia.

Women with elevated insulin levels develop PCOS more quickly. Loss of weight has been shown to have an encouraging effect on endocrine and ovarian function. When excess fat is burned off, the body's hormones are balanced, inflammation is reduced, insulin sensitivity is enhanced, and androgens, particularly testosterone and androstenedione, are greatly reduced [49]. Although a 10% weight loss would be ideal, even a 5% weight loss has been shown to assist people with PCOS in getting their periods back on track. Both overweight and underweight individuals with PCOS had higher blood insulin levels than healthy controls with similar body mass indices.

High insulin levels are triggered by a permutation of insulin resistance, poor insulin clearance, and persistent insulin production. However, the protective effect of a normal menstrual cycle on insulin resistance and sensitivity differs among women [50].

Hyperinsulinemia increases ovarian androgen secretion through the increase of insulin-like growth factor-I (IGF-1) and insulin-like growth factor-2 (IGF-2), which are two crucial controllers of ovarian follicular evolution and steroidogenesis [51]. IGFBP-1 is secreted by the liver, and its inhibition increases IGF-1 and IGF-2 levels. Ovarian androgen synthesis and excretion are further amplified by hepatic IGF-1 and IGF-2, which act on IGF-1 receptors, in addition to IGF-2 release from theca cells. Another factor contributing to hyperandrogenism outside of the ovaries is hyperinsulinemia. There is a strong correlation between elevated LH secretion and weight development and between elevated androgen release from the ovaries and weight loss.

Excessive levels of local ovarian androgen are exacerbated by hyperinsulinemia, leading to anovulation and early follicular atresia. The epidemiology of polycystic ovary syndrome has revealed a possible hereditary component. Two regions of the genome have been linked to PCOS [52]. The dinucleotide repeat microsatellite marker D19S884 in intron 55 of the fibrillin 3 gene and follistatin gene are two such genes. These genes share a TGF-binding site, and both control TGF action in other parts of the TGF superfamily.

However, the fibrillin 3 gene microsatellite D19S884 polymorphism is also strongly linked to polycystic ovary syndrome. Patients affected by polycystic ovary syndrome (PCOS) have been shown to experience a growing risk of cardiovascular disease as well as infertility due to TGF- dysregulation [53].

Negative Impact of PCOS on Cardiovascular Disease:
An insulin-resistant environment may account for the elevated risk of CVD observed in people with PCOS [54]. Women with polycystic ovarian syndrome (PCOS) had elevated low-density lipoprotein (LDL) cholesterol, reduced high-density lipoprotein (HDL) cholesterol, and increased triglyceride-rich lipoprotein (TGL) levels; [55]. Triglyceride and high-density lipoprotein (HDL) levels in women serve as independent predictors of mortality from CVD. Obesity, high insulin levels, and increased blood pressure all add to an increased risk of

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CVD. Abnormal fat distribution and/or excessive visceral fat have been associated with insulin resistance and metabolic problems in some PCOS patients with a normal body mass index [56]. A higher total body fat percentage has been found to increase the risk of CVD among healthy women and is a major contributor to insulin resistance.

A high fat mass is linked to a surge in proinflammatory cytokines, which may increase the risk of cardiovascular disease in females without polycystic ovarian syndrome. Heart disease and death are both more likely in people with an abnormal lipid profile, as reported [57]. Losing weight improves heart rate recovery in overweight PCOS women because it decreases production of many inflammatory markers and cytokines that increase the risk of cardiovascular issues. These markers often imply a considerable reduction in adiponectin levels and an amplified threat of endothelial malfunction [58].

The considerable increase in CVD risk in PCOS-affected women of normal weight may be due to oxidative stress, which is categorized by increased reactive oxygen species (ROS) and decreased antioxidant levels. Factors such as abdominal obesity, advanced age, hypertension, increased blood glucose, insulin, triglyceride, and insulin resistance have all been associated with increased oxidative stress. All of the aforementioned factors can increase one's chance of developing CVD. A decrease in antioxidant capability in the cardiovascular, excretory, and nervous systems underlies the development, progression, and clinical manifestations of cardiovascular disease (CVD) [59].

Cancer and PCOS:

It has been widely contested for more than 60 years whether polycystic ovary syndrome (PCOS) causes the progression of ovarian, endometrial, or breast malignancies. Endometrial cancer, the most frequently reported cancer in women with PCOS, is caused by prolonged exposure of tissues to unopposed estrogen. Several further studies seem to substantiate this link. Oxidative stress is essential for the growth and spread of cancer, and chronic inflammation can develop without treatment [60].

Increased endometrial cancer risk and worsening of PCOS have been connected to visceral fat intake, insulin resistance and abdominal obesity. PCOS is characterized by an abnormal menstrual cycle, inability to ovulate, and infertility. Endometrial hyperplasia and cancer are aided by prolonged exposure to high levels of unopposed estrogen.

Women with PCOS are more prone to developing cancer due to a shift in blood chemistry resulting from insulin resistance. This shift may encourage the secretion of androgens, LH, and IGF-1. [61]

Treatment:

Two methods of treatment are generally accepted worldwide:

1. Non-Pharmacological: Weight loss that is achieved without the use of pharmaceuticals can be achieved by adopting a lower caloric intake diet and increasing physical activity. Even a modest weight loss of approximately 5% could have significant health benefits. Finally, regular habits of going to bed early and getting up early should be preserved. In other words, significant progress is achieved by maintaining healthy practices. It is also important to preserve mental health by making time for hobbies such as listening to music, singing, or playing sports [62,63,64].

2. Pharmacological: Pharmacological refers to treatments that utilize medication. Metformin (which decreases insulin levels and enhances insulin sensitivity) is commonly given for continuing ovulation [65, 66, 67, 68, 69]. If pregnancy is still not found after clomiphene administration, additional supplementation with metformin is recommended since it prevents the onset of type 2 diabetes and promotes weight loss [70]. In combination with progesterone, birth control pills suppress testosterone production while maintaining estrogen regulation [71,72,73]

3. Non-Pharmacological:

a) Reforms in Lifestyle: Maximum females with PCOS are overweight or obese, therefore losing weight is a top recommendation. Eating right and exercising regularly can both aid digestion and boost insulin sensitivity, which can lead to significant weight loss [74]. Patients with PCOS often struggle with high blood cholesterol levels, hormonal imbalances, and obesity; losing weight in this population requires more than just exercise. Women in India often ignore the importance of a balanced diet, which should include enough protein

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and fiber. Weight loss is possible according to scientific studies. Due to uneven ovulation and an increased understanding of ovulation induction medicines, the number of births and rate of pregnancy in females with PCOS who have experienced infertility have increased. According to previous studies [75], losing as little as 5% of one's starting weight can lead to a woman's reaction to ovulation and reproductive drugs, hence restoring regular menstruation.

b) Laparoscopic ovarian drilling: Ovarian drilling is a type of laparoscopic surgery that involves making several holes in the surface of the ovaries and stroma. It is hypothesized that this treatment will reduce androgen levels by destroying the tissue that generates androgens. The chance of having more than one child is reduced, and various studies have revealed that this approach is as effective as medical interventions [76].

Pharmacological:

A. Herbal drugs that are effective in treating PCOS:

1. Mentha spicata: This moth is commonly known as garden mint, common mint or spearmint and is included in the Lamiaceae family. Its active constituent is β-bromobenzene (PubChem CID 324224), which has shown potential therapeutic efficacy against PCOS through the suppression of testosterone and the restoration of follicular growth in ovarian tissue. [77,78,79]

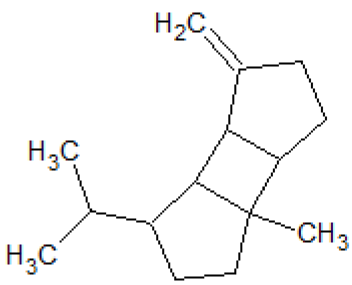

Fig. 4: **β-**Borbonene: 3a-methyl-6-methylidene-1-(propan-2-yl)decahydrocyclopenta[3,4]cyclobuta[1,2]cyclopentene

2. Cinnamonium zeylancum: This plant is commonly referred to as cinnamon and belongs to the Lauraceae family. Cinnamaldehyde (PubChem CID 637511) is an active component. This treatment has been shown to improve the menstrual cycle and to have an insulin-sensitizing impact on people with PCOS [80].

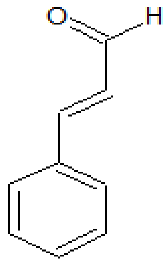

Fig. 5: **Cinnamaldehyde**: (2*E*)-3-phenylprop-2-enal

3. O. majorana: O. majorana is a perennial herb or undershrub that is sensitive to cold weather and belongs to the Lamiaceae family. Its active ingredient α-terpineol (PubChem CID 17100) has the potential to increase insulin sensitivity and lower adrenal androgen levels in the hormonal profiles of women with PCOS [81].

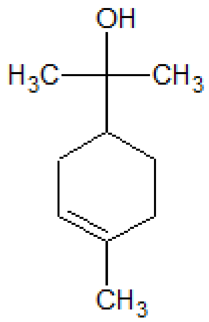

Fig. 6: **α-Terpineol**: 2-(4-methylcyclohex-3-en-1-yl)propan-2-ol

4. Trigonella foenum-graceum L: This genus is frequently referred to as fenugreek and belongs to the Fabaceae family. Its active ingredient, steroidal sapponins, is used to treat infertility caused by PCOS [82].

5. Phoenix dactylifera: This plant is also named Date Palm and is a member of the Arecaceae family. Protocatechuic acid (PubChem CID 72) is one of its active constituents and helps reduce insulin resistance and diabetes complications in patients with PCOS [83,84].

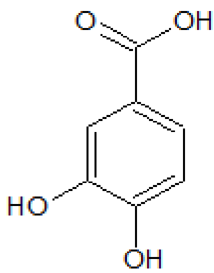

Fig. 7: **Protocatechuic acid**: 3,4-dihydroxybenzoic acid

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6. Berberine: Berberine (PubChem CID 2353) is an isoquinoline alkaloid. Research studies point to the potential of berberine for balancing hormones, particularly in the case of PCOS. Phenolic acid can benefit greatly from berberine, as indicated by enhanced fertility, loss of body weight and decreased inflammation. Due to its impact on body composition and lipid profiles and its ability to enhance hormone status, berberine may have greater potential to lower the incidence of CVD in PCOS patients than metformin [85].

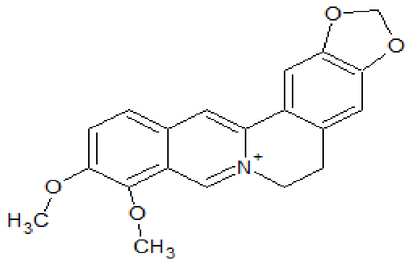

Fig. 8: **Berberine**: 16,17-dimethoxy-5,7-dioxa-13-azoniapentocyclo[11.8.0.$0^{2,10}$.$0^{4,8}$.$0^{15,20}$]henicosa-1(13),2,4(8),9,14,16,18,20-octaene.

PRESCRIPTION MEDICATIONS USED TO TREAT PCOS:

1. **Anovulation**:

Clomiphene (PubChem CID 1548955): This is the preferred medication for teenagers who suffer from polycystic ovarian syndrome. Clomiphene acts as an antiestrogen by binding to estrogen receptors in the brain, increasing the pulse frequency in the anterior pituitary region of GnRH, and promoting the formation of follicle-stimulating hormone (FSH). It is typically administered for 5 consecutive days in the middle of the 2nd and 5th days of the menstruation period, starting at 50 mg/day and progressively increasing to 150 mg/day. Adverse effects include hot flashes, bloating, exhaustion, numerous births, hyperstimulation syndrome, ovarian expansion, and symptoms of hot flashes [86].

2. **Antidiabetic agents**:

Diabetes medications are generally given to improve fertility, reduce insulin resistance and lower circulating levels of androgen.

Liraglutide (PubChem CID 16134956): Patients with type II diabetes and obesity were treated with this glucon-like peptide receptor I agonist. Liraglutide was utilized to cause a considerable weight decrease in PCOS-affected women [87,88].

Myo-inositol or D-chiro-inositol (PubChem CID 892): These chemicals work as secondary messengers in the insulin signaling process and are insulin-sensitizing agents. It also has the ability to correct hormonal imbalances [89, 90, 91].

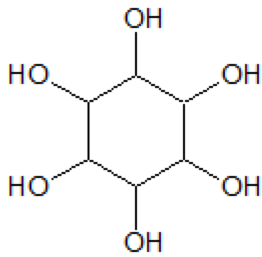

Fig. 9: **Myo-inositol**: cyclohexane-1,2,3,4,5,6-hexol

Metformin (PubChem CID 4091): It is the medication that these individuals use the most frequently to manage their metabolism. In women with PCOS, the pharmacological effects of metformin, such as insulin sensitizing and hypoglycemic effects, have been thoroughly demonstrated [92,93,94]

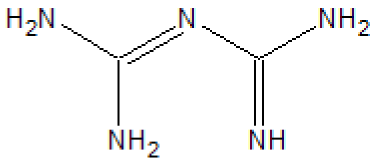

Fig. 10: Metformin: 2-carbamimidoylguanidine

4. **Gonadotropins:**

For women with PCOS who do not ovulate, gonadotropin treatment can be considered a second-line option if they have not responded to first-line oral ovulation stimulation medications, such as SERM and aromatase inhibitors.

5. **Aromatase Inhibitors:**

Letrozole, an aromatase inhibitor, was used to induce ovulation, but the results were not statistically significant. It was permitted for the treatment of hormone-responsive breast cancer.

6. **Anti-androgens**

Spironolactone, finasteride and flutamide are antiandrogens that reduce androgen levels in patients with PCOS. These anti-androgens can increase the lipid profile, which is often high in PCOS patients.

7. Oral contraceptives:

In treating PCOS, oral contraceptives (OCs) act by regulating menstruation and decreasing androgen levels.

8. Statins:

Statins may play a vital role in the treatment of PCOS since they can reduce testosterone levels, in addition to LDL-C, triglyceride, and total cholesterol levels [95].

CONCLUSION

Hormonal dysregulation, ovarian dysfunction, and metabolic abnormalities all play a role in PCOS, complicating its endocrine function. The complex etiology of PCOS has been illuminated by the new science of epigenetics. Dysregulation of genes and pathways in PCOS has been linked to epigenetic alterations such as DNA methylation, histone modifications, and noncoding RNAs. New insights into the etiology of PCOS and the possibility of developing specific therapeutic methods could be gained by studying the epigenetic contributions to this disorder.

Polycystic ovarian syndrome is extremely multifaceted and necessitates a wide variety of therapeutic approaches. Women find this frustrating, management clinicians often find it demanding, and researchers have a scientific challenge when attempting to understand it. Given the rapid pace at which PCOS research is progressing, it is essential that the findings be translated to knowledge and action by women and healthcare professionals. Every woman needs to have her awareness raised.

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Conflict of interest:

The authors declares that there is no conflict of interest.

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