

Review

Polycystic Ovary Syndrome and Reproductive Health: A Comprehensive Review

Ramadan S. Hussein^{1,*}, Salman Bin Dayel¹, Othman Abahussein¹¹Department of Internal Medicine, College of Medicine, Prince Sattam Bin Abdulaziz University, 11942 Al-Kharj, Saudi Arabia*Correspondence: ramadangezera@yahoo.com (Ramadan S. Hussein)

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Abstract

Objectives: Polycystic ovary syndrome (PCOS) is a prevalent and intricate endocrine disorder that impacts women of reproductive age. It is marked by various symptoms, including menstrual irregularities, hyperandrogenism, and metabolic dysfunctions, with significant implications for reproductive and overall health. This review aims to provide a comprehensive analysis of the impact of PCOS on reproductive health, highlighting the underlying pathophysiology, clinical manifestations, and emerging therapeutic approaches. **Mechanism:** The current literature was detailed, focusing on the hormonal imbalances associated with PCOS, including androgen excess, insulin resistance, and dysregulation of the hypothalamic-pituitary-ovarian (HPO) axis. The review also explored genetic and environmental factors contributing to PCOS and described the characteristic ovarian morphology. **Findings in Brief:** The findings reveal that PCOS is not only a leading cause of infertility but also contributes to a spectrum of metabolic and psychological issues. Recent research highlights the role of inflammation, the gut microbiome, and novel therapies in managing PCOS. Despite advances, gaps in understanding the long-term implications of PCOS on reproductive health remain. **Conclusions:** The review underscores the need for individualized and holistic treatment strategies in managing PCOS, integrating emerging therapies and mental health support. Continued research is vital to improving patient outcomes and advancing the management of this multifaceted condition.

Keywords: PCOS; reproductive health; hormonal imbalance; ovarian function; menstrual irregularities; infertility

1. Introduction

Polycystic ovary syndrome (PCOS) is among the most prevalent endocrine disorders affecting women of reproductive age, with an estimated prevalence ranging from 8% to 13% globally [1]. This condition is marked by a variety of symptoms, such as hyperandrogenism, irregular menstrual cycles, and polycystic ovaries, which collectively contribute to a wide range of reproductive and metabolic complications [2]. PCOS not only impacts fertility but also poses long-term health risks, including type 2 diabetes, cardiovascular disease (CVD), and psychological challenges, making it a significant public health concern [3].

This review provides a comprehensive overview of PCOS's impact on reproductive health. The article aims to synthesize recent findings on the pathophysiology of PCOS, its associated reproductive complications, and the latest management strategies. By exploring these aspects, the review seeks to offer insights into the challenges faced by women with PCOS and the advancements in therapeutic interventions.

This review is structured into several key sections: first, an exploration of the underlying pathophysiology of PCOS and its implications for reproductive health; second, an examination of the reproductive complications, including infertility and pregnancy-related risks; and finally, a discussion of the current management strategies, encompassing both lifestyle modifications and medical treatments,

aimed at improving reproductive outcomes in women with PCOS.

2. Pathophysiology of PCOS

2.1 Hormonal Imbalances

The pathophysiology of PCOS is complex and involves a combination of hormonal imbalances, most notably hyperandrogenism, insulin resistance, and dysregulation of the hypothalamic-pituitary-ovarian (HPO) axis [4]. One emerging area of interest is the role of kisspeptin, a peptide involved in reproductive hormone regulation, which has shown relevance in linking metabolic and reproductive aspects of PCOS. Kisspeptin is a peptide that regulates the release of gonadotropin-releasing hormone (GnRH), which influences luteinizing hormone (LH) secretion. In women with PCOS, kisspeptin signalling is often dysregulated, leading to abnormal GnRH and LH release patterns. Since elevated LH levels are a common characteristic of PCOS, this impaired kisspeptin signalling is believed to be one of the contributors to the hormonal imbalances observed in the condition [5].

Additionally, PCOS is frequently associated with insulin resistance, and there is evidence that insulin resistance may further affect kisspeptin levels [5]. This creates a feedback loop where insulin resistance and altered kisspeptin signalling intensify reproductive and metabolic issues. In PCOS, elevated insulin levels may reduce kisspeptin activ-



ity, which disrupts GnRH pulsatility and promotes an abnormal increase in LH levels, contributing to hyperandrogenism (increased androgen production) [5].

Moreover, insulin resistance can lead to compensatory hyperinsulinemia, characterized by elevated insulin levels that exacerbate hyperandrogenism. Insulin plays a crucial role in reducing the production of sex hormone-binding globulin (SHBG), thereby increasing the bioavailability of circulating androgens. Furthermore, insulin resistance can disrupt normal follicular development and ovulation, contributing to the reproductive dysfunction commonly seen in PCOS. Clinically, the presence of insulin resistance is linked to an increased risk of metabolic disorders, such as type 2 diabetes mellitus (T2DM) and CVD, making its recognition and management vital in the clinical setting for women with PCOS [6].

Poznan and Modena research groups have emphasized the link between kisspeptin, insulin, and metabolic dysfunction in PCOS, suggesting that kisspeptin could act as a mediator between metabolic and reproductive health [5]. By influencing insulin and LH levels, kisspeptin may contribute to both the metabolic symptoms (such as insulin resistance) and the reproductive symptoms (such as irregular ovulation and high androgen levels) seen in PCOS [5]. This connection between kisspeptin, metabolism, and reproductive function makes kisspeptin a potential target for new therapies aimed at treating both the hormonal and metabolic aspects of PCOS [5].

Elevated LH and insulin levels synergistically stimulate the ovarian theca cells to produce more androgens. These androgens disrupt normal follicular development, resulting in anovulation, irregular menstrual cycles, and the characteristic polycystic ovaries. Clinically, hyperandrogenism presents as hirsutism, alopecia, and acne [3]. The HPO axis, which controls reproductive hormone release and ovulation, is often dysregulated in PCOS. This dysregulation typically involves an increased frequency of GnRH pulses, leading to a higher ratio of LH to follicle-stimulating hormone (FSH). Elevated LH stimulates ovarian androgen production, while insufficient FSH hampers normal follicular development, contributing to anovulation and infertility. The disrupted feedback loop between the ovaries and the hypothalamus/pituitary further perpetuates the hormonal imbalances seen in PCOS [6].

2.2 Genetic and Environmental Factors

PCOS is believed to be a multifactorial disorder, with both genetic and environmental factors playing significant roles. Several studies have identified a familial clustering of PCOS, suggesting a significant genetic component [6,7]. Genome-wide association studies (GWAS) have identified multiple susceptibility loci related to reproductive and metabolic pathways [1,7]. However, the exact genetic mechanisms remain unclear, and multiple genes likely interact with environmental factors to increase the

risk of developing PCOS [7]. Environmental factors, such as lifestyle, diet, and prenatal exposures, significantly influence the manifestation of PCOS. For instance, obesity exacerbates insulin resistance and hyperandrogenism, worsening PCOS symptoms [1]. Moreover, prenatal androgen exposure has been hypothesized to predispose individuals to PCOS, potentially by programming the HPO axis and increasing susceptibility to hyperandrogenism later in life [8].

2.3 Ovarian Morphology

The characteristic appearance of polycystic ovaries is one of the defining features of PCOS. PCOS are defined by the presence of numerous small follicles (usually 12 or more) that fail to mature and ovulate. These follicles accumulate in the ovaries, often causing them to enlarge. The exact mechanism leading to this ovarian morphology involves the disruption of normal follicular development due to hormonal imbalances, particularly the excess production of androgens and insufficient FSH levels [9]. The presence of polycystic ovaries, as observed via ultrasound, is a key diagnostic criterion for PCOS (as per the Rotterdam criteria) [10]. However, it is important to note that polycystic ovaries do not always indicate PCOS and not all women with PCOS exhibit polycystic ovaries. The ovarian morphology in PCOS contributes to the clinical manifestations of the syndrome, particularly anovulation and the associated infertility [1]. This combination of hormonal, genetic, and environmental factors underpins the pathophysiology of PCOS, leading to its diverse clinical presentation and associated reproductive and metabolic complications [10].

3. Clinical Manifestations of PCOS

3.1 Menstrual Irregularities

A key characteristic of PCOS is menstrual irregularity, which includes oligo-ovulation, anovulation, and amenorrhea. In women with PCOS, oligo-ovulation (infrequent ovulation) and anovulation (absence of ovulation) are common due to hormonal imbalances that disrupt the normal menstrual cycle. These disruptions result from the excessive production of androgens and the altered secretion of gonadotropins, specifically a higher LH to FSH ratio, which impairs follicular development [7,10]. Consequently, women with PCOS may experience irregular menstrual cycles, with intervals exceeding 35 days, or have fewer than eight menstrual periods per year. These ovulatory disturbances are the primary cause of infertility in women with PCOS [10]. Amenorrhea, or the absence of menstrual periods for six months or longer, can occur in more severe cases of PCOS. It is often linked to prolonged anovulation and can increase the risk of endometrial hyperplasia and carcinoma due to unopposed estrogen exposure. The presence of amenorrhea, especially when combined with other symptoms such as hirsutism, should prompt consideration of PCOS as a potential diagnosis [11].

3.2 Hyperandrogenism

Hyperandrogenism, marked by elevated androgen levels, is a central feature of PCOS and manifests in various clinical signs, significantly affecting the quality of life of those impacted. Hirsutism, or excessive hair growth in regions where men typically develop hair (such as the face, chest, and back), is one of the most common clinical manifestations of hyperandrogenism in PCOS. It affects approximately 60–70% of women with the syndrome [9,12]. Hirsutism can have a significant psychosocial impact, leading to reduced self-esteem, anxiety, and depression. The extent of hirsutism severity is often assessed using the Ferriman-Gallwey scoring system [12]. Acne is another common manifestation of hyperandrogenism in PCOS, affecting about 20–30% of women with the condition. Elevated androgen levels increase sebaceous gland activity, leading to the development of acne. The persistence of acne into adulthood, particularly severe forms, is often a clinical indicator of underlying hyperandrogenism. Like hirsutism, acne can adversely affect self-image and mental health [6]. Androgenic alopecia, or male-pattern hair loss, is a less common but distressing symptom of PCOS. It typically presents as thinning hair on the scalp, particularly at the crown. While less frequently observed than hirsutism and acne, androgenic alopecia can be psychologically devastating, contributing to a negative body image and emotional distress [12].

3.3 Metabolic Symptoms

PCOS is closely linked with several metabolic disturbances, most notably insulin resistance and obesity, which have significant implications for long-term health. Insulin resistance, a condition where the body's cells become less responsive to insulin, affects 50–80% of women with PCOS. It is particularly common among those who are obese or overweight. Insulin resistance contributes to hyperinsulinemia, which exacerbates hyperandrogenism and further disrupts ovarian function [9]. Over time, insulin resistance raises the risk of T2DM and CVD, making it a critical aspect of PCOS management [13]. Obesity is prevalent in 40–80% of women with PCOS and significantly aggravates both the reproductive and metabolic aspects of the condition. Obesity exacerbates insulin resistance and hyperandrogenism, leading to more severe menstrual irregularities and higher risks of infertility. Furthermore, obesity in PCOS is linked to an increased risk of metabolic syndrome, dyslipidemia, hypertension, and non-alcoholic fatty liver disease (NAFLD) [14]. The metabolic disturbances associated with PCOS, particularly insulin resistance and obesity, elevate the risk of various long-term health problems, such as T2DM, cardiovascular disease, and endometrial cancer. The management of these metabolic symptoms is crucial to reducing the overall morbidity associated with PCOS and enhancing the quality of life for the women affected [15,16]. These clinical manifestations highlight the

broad spectrum of symptoms associated with PCOS and underscore the need for holistic management strategies that consider both the reproductive and metabolic aspects of health.

4. Impact of PCOS on Reproductive Health

4.1 Infertility

PCOS is a common cause of infertility due to its impact on ovulation and egg quality. Women with PCOS often experience anovulation, meaning their ovaries do not release eggs regularly. This lack of ovulation is primarily due to hormonal imbalances, including elevated levels of LH and androgens, which disrupt the normal ovarian cycle [6]. Additionally, the quality of oocytes (eggs) in women with PCOS may be compromised due to irregular or absent ovulation, further affecting their ability to conceive. The presence of multiple small cysts in the ovaries, while not directly causing infertility, is a hallmark of the condition that reflects the underlying hormonal dysfunction [7]. Lifestyle factors play a significant role in the management of infertility in women with PCOS. Weight management, dietary modifications, and physical activity can positively influence insulin sensitivity and hormonal balance, thereby improving ovulatory function. Studies have shown that even modest weight loss can restore regular ovulation in some women, enhancing their chances of conception [7,9]. Furthermore, lifestyle interventions can improve overall metabolic health, which is crucial for women with PCOS who are at higher risk for conditions such as T2DM and CVD. Therefore, addressing lifestyle factors is an integral part of infertility treatment in women with PCOS, highlighting the importance of a holistic approach to managing this complex condition [7,9].

4.2 Pregnancy Outcomes

Pregnant women with PCOS carry a higher risk of various complications. Miscarriage rates are higher due to factors like hormonal imbalances and potential issues with the uterine lining. Gestational diabetes, marked by elevated blood sugar levels during pregnancy, is more prevalent among women with PCOS [17]. Additionally, these women are at a higher risk for preeclampsia, a condition that can lead to elevated blood pressure and damage vital organs including the kidneys and liver. The increased risk of these complications necessitates vigilant monitoring and management throughout pregnancy to protect the health of both the mother and the baby [18].

4.3 Long-Term Reproductive Risks

Beyond immediate pregnancy-related issues, PCOS is linked to several long-term reproductive health risks. Women with PCOS are at a higher risk of endometrial hyperplasia, a condition where the lining of the uterus becomes abnormally thick. This can be a precursor to endometrial cancer if left untreated. The irregular shedding

Table 1. Diagnostic criteria and assessment tools for PCOS.

Section	Criteria/tool	Details
5.1 Diagnostic criteria	Rotterdam criteria (2003)	Requires at least two of the following: 1. Oligo- or anovulation; 2. Clinical or biochemical signs of hyperandrogenism; 3. Polycystic ovaries visible on ultrasound; Emphasizes that PCOS is heterogeneous and can vary in presentation.
	National Institutes of Health (NIH) criteria (1990)	Requires both of the following: 1. Clinical or biochemical signs of hyperandrogenism; 2. Oligo- or anovulation; Does not require polycystic ovaries on ultrasound.
	Androgen Excess Society (AES) criteria (2006) [20,21]	Requires all of the following: 1. Clinical or biochemical signs of hyperandrogenism; 2. Oligo- or anovulation; 3. Exclusion of other conditions causing hyperandrogenism; Focuses on ruling out other possible diagnoses.
5.2 Assessment tools	Ultrasound	Transvaginal ultrasound to identify polycystic ovaries with multiple small cysts along the ovary's periphery.
	Hormonal assays (androgens) [22–24]	Blood tests to measure hormone levels such as androgens (T, androstenedione, 17OHP), LH, and FSH. Elevated androgens and abnormal LH/FSH ratios are indicative of PCOS.
	Other diagnostic tests	Includes glucose tolerance tests for insulin resistance or diabetes, and endometrial biopsy for endometrial hyperplasia symptoms.
5.3 Differential diagnosis [27–29]	Thyroid disorders	Conditions like hypothyroidism or hyperthyroidism cause menstrual irregularities and weight changes.
	Adrenal disorders	Conditions such as congenital adrenal hyperplasia presenting with hyperandrogenism and menstrual irregularities.
	Primary ovarian insufficiency	Presents with amenorrhea and elevated gonadotropins. Distinguishable from PCOS with FSH and estradiol testing.
	Hyperprolactinemia [25,26]	Elevated prolactin levels cause menstrual irregularities and hyperandrogenism symptoms. Requires prolactin testing and pituitary imaging.

PCOS, polycystic ovary syndrome; LH, luteinizing hormone; FSH, follicle-stimulating hormone; T, 1-testosterone; 17OHP, 17-hydroxyprogesterone.

of the endometrial lining, due to infrequent or absent menstrual cycles, contributes to this risk [16]. Regular monitoring and management of menstrual irregularities are essential to mitigate these long-term risks and maintain reproductive health [16,19]. Understanding these aspects of PCOS is essential for effectively managing the condition and enhancing overall reproductive health outcomes.

5. Diagnostic Criteria and Evaluation

Accurate diagnosis of PCOS requires a comprehensive evaluation that considers clinical presentation, laboratory findings, and imaging results. Here is a Table 1 (Ref. [20–29]) that organizes the diagnostic criteria, assessment tools, and differential diagnosis for PCOS.

6. Management of PCOS and Reproductive Health

6.1 Lifestyle Interventions

Weight loss can significantly improve insulin sensitivity and reduce androgen levels for women with PCOS. Even a modest reduction in body weight, around 5–10%, can assist in regulating menstrual cycles, enhancing ovulation, and reducing symptoms like acne and hirsutism. A balanced diet plays a crucial role in managing insulin resistance and alleviating symptoms of conditions like PCOS, and specific dietary recommendations can enhance this effect. Incorporating high-fiber foods rich in soluble and insoluble fiber, such as fruits, vegetables, legumes, and whole grains, can slow the absorption of sugar and improve insulin sensitivity. Additionally, emphasizing low glycemic index (GI) foods, which have a minimal impact on blood sugar levels—such as whole grains, non-starchy vegetables, nuts, and seeds—can be particularly beneficial. Including sources of lean protein, such as chicken, fish, tofu, and legumes, helps maintain muscle mass and supports metabolic health [24,30]. Moreover, incorporating healthy fats from sources like avocados, olive oil, and fatty fish can reduce inflammation and further improve insulin sensitivity. Finally, limiting the intake of refined carbohydrates, such as white bread, pastries, and sugary snacks, as well as added sugars, is essential for controlling blood sugar levels and managing insulin resistance effectively [7,24,30]. Regular physical activity also plays a critical role in improving insulin sensitivity, aiding weight management, and enhancing overall reproductive health. Both aerobic exercises and resistance training are recommended [30]. Together, these lifestyle interventions form a comprehensive approach to managing PCOS, particularly in addressing insulin resistance and its related complications.

6.2 Pharmacological Treatments

6.2.1 Hormonal Therapies

Birth control pills are commonly used to regulate menstrual cycles, reduce androgens, and improve acne and hirsutism.

They work by suppressing ovarian function and decreasing circulating testosterone. Medications like spironolactone can be used to manage symptoms of excess androgen, such as hirsutism and acne. They work by blocking androgen receptors and decreasing testosterone production. In some cases, other hormonal therapies like progestins or estrogens may be used to manage menstrual irregularities [27].

6.2.2 Insulin Sensitizers

Metformin is a widely used insulin-sensitizing medication for managing PCOS. It works by enhancing insulin sensitivity, reducing hepatic glucose production, and improving peripheral glucose uptake, which helps to mitigate insulin resistance. As a result, metformin can be particularly beneficial for women with PCOS who exhibit insulin resistance or compensatory hyperinsulinemia, rather than being universally recommended for all PCOS patients. Metformin has been associated with improvements in menstrual regularity and ovulation, which can aid in alleviating some reproductive symptoms of PCOS [27]. Additionally, thiazolidinediones, such as pioglitazone, are another class of insulin-sensitizing drugs that can improve insulin sensitivity, though they are less commonly used due to potential side effects, including weight gain and cardiovascular risks [27,28].

6.2.3 Ovulation Induction

Clomiphene citrate, the first-line treatment for inducing ovulation in women with PCOS works by blocking estrogen receptors in the hypothalamus, leading to increased release of FSH and LH, ultimately stimulating ovulation. In contrast, letrozole, an aromatase inhibitor, reduces estrogen production by inhibiting the enzyme aromatase, which converts androgens to estrogens. This decrease in estrogen levels triggers a compensatory rise in FSH, promoting follicular development and ovulation. Letrozole may be more effective than clomiphene for some women with PCOS, particularly those who are resistant to clomiphene, and has a different side effect profile, making it a valuable alternative [28,29]. Gonadotropins, injectable hormones such as FSH and LH can be used for ovulation induction in cases where oral medications are ineffective [7,29].

6.2.4 Surgical Options

Ovarian drilling, this laparoscopic procedure involves making small holes in the ovaries with a laser or electrical current to reduce androgen production and restore ovulation. It is typically considered for women who have not responded to other treatments [2,7].

6.2.5 Assisted Reproductive Technologies (ART)

Intracytoplasmic sperm injection (ICSI), can be an option for women with PCOS who have not achieved pregnancy with other treatments. It involves stimulating the

ovaries to produce multiple eggs, retrieving them, fertilizing them in a lab, and transferring the embryos into the uterus. Other ART options techniques such as intrauterine insemination (IUI) may also be used, especially if there are additional fertility issues or if the woman has a partner with male factor infertility [17].

Management of PCOS often requires a multi-faceted approach tailored to the individual's symptoms, reproductive goals, and overall health. Collaboration between patients and healthcare providers is essential to optimize treatment outcomes.

7. Psychological and Emotional Impact of PCOS

7.1 Mental Health Issues

PCOS has profound psychological and emotional effects, which often go hand in hand with its physical manifestations. Women with PCOS are at an increased risk for several mental health issues, including anxiety, depression, and body image disturbances. Studies have shown that women with PCOS are more likely to experience anxiety and depression than those without the condition [29,31]. This vulnerability to depression may be partly explained by hormonal and metabolic factors linked to PCOS. Elevated androgen levels and insulin resistance, both common in PCOS, have been associated with mood disturbances and altered emotional regulation [3,29].

Additionally, neurosteroids, which are steroid hormones synthesized in the brain and have mood-regulating functions, may play a role in this increased susceptibility. In PCOS, insulin resistance can impact adrenal function, leading to imbalances in neurosteroids that further contribute to depressive symptoms. The physical manifestations of PCOS—such as weight gain, hirsutism, acne, and hair loss—can severely affect body image and self-esteem, heightening the risk of body dissatisfaction and social anxiety [3,31]. This, combined with fertility concerns and societal pressures related to appearance, often results in decreased participation in social activities and a lowered overall quality of life [31]. Depression is particularly prevalent, with some studies indicating that women with PCOS have a nearly double risk of depression compared to those without PCOS [32]. This may be related to hormonal imbalances, particularly elevated androgen levels, which have been linked to mood disturbances [31,32]. The societal pressure to conform to certain standards of beauty further exacerbates these issues, often leading to social withdrawal and decreased participation in everyday activities [32].

7.2 Counseling and Support

Addressing the psychological and emotional impact of PCOS is critical to the comprehensive management of the condition. Psychological support, counselling, and patient education play essential roles in helping women cope with the mental health challenges associated with PCOS. Psy-

chological support, including cognitive-behavioural therapy (CBT), is effective in managing the mental health symptoms of PCOS. CBT can help women develop healthier coping mechanisms, challenge negative thought patterns, and improve their overall mood and functioning [28,33]. Regular psychological counselling can provide a safe space for women to discuss their concerns, fears, and frustrations related to PCOS [33,34].

Educating patients about PCOS and its effects on both physical and mental health is crucial. A better understanding of the condition can help reduce anxiety and empower women to take an active role in managing their health. Education should also include information on the importance of lifestyle changes, such as diet and exercise, which can improve both physical symptoms and mental well-being [35].

Participation in support groups, either in-person or online, can provide additional emotional support. Connecting with others who have PCOS can help reduce feelings of isolation, offer practical advice, and create a sense of community. These groups can be particularly beneficial in helping women share experiences and strategies for coping with the various aspects of PCOS [36].

In summary, the psychological and emotional impact of PCOS is significant and multifaceted. Addressing these aspects through psychological support, counselling, and patient education is vital for improving the overall quality of life for women with PCOS.

8. Emerging Research and Future Directions

8.1 Recent Advances

Recent research in PCOS has significantly enhanced our understanding of the condition's complex pathophysiology and its broader health implications. Studies have increasingly focused on the role of chronic low-grade inflammation in PCOS, which may contribute to both metabolic and reproductive abnormalities [37,38]. Additionally, advances in genetic studies have identified specific genetic loci associated with PCOS, offering new insights into the heritability and molecular mechanisms underlying the syndrome [7,38]. Recent research has also explored the gut microbiome's influence on PCOS, suggesting that dysbiosis may play a role in the syndrome's metabolic manifestations. Moreover, advancements in imaging techniques, such as advanced ultrasonography, have improved the ability to diagnose and monitor the morphological changes in ovaries more precisely [39].

8.2 Potential Therapies

Several novel therapeutic approaches for managing PCOS are currently under investigation, offering promising avenues for treatment. Inositol isomers, particularly Myo-inositol and D-chiro-inositol, are of particular interest due to their insulin-sensitizing properties, which can help manage both the metabolic and reproductive symptoms of

PCOS. Research suggests that these isomers play a key role in modulating insulin sensitivity, with Myo-inositol primarily supporting insulin signalling pathways, and D-chiro-inositol aiding in androgen reduction and ovarian function improvement. Their efficacy may vary depending on individual metabolic profiles; for instance, women with family histories of diabetes or liver impairment may exhibit altered insulin sensitivity and heightened androgen excess due to impaired aromatase expression [40]. These factors should be considered when selecting the most appropriate inositol for therapy, as highlighted by Genazzani AD and Genazzani AR (2023) [41], who emphasize the importance of personalized inositol integration based on specific metabolic dysfunctions such as familial diabetes and liver issues [40]. Additionally, as the role of inflammation in PCOS becomes more evident, anti-inflammatory therapies, including omega-3 fatty acids and specific anti-inflammatory drugs, are being explored for their potential to alleviate symptoms [42]. Another emerging area of interest is the modulation of gut microbiota through probiotics and prebiotics, which could restore a healthy gut balance, thereby improving metabolic health and reducing insulin resistance in women with PCOS [39]. Advances in genetic research have also opened the door to gene therapy and personalized medicine strategies tailored to an individual's genetic makeup, offering the possibility of more precise and effective treatments [38]. Furthermore, new pharmacological agents targeting the androgen receptor and insulin signalling pathways are being developed and tested in clinical trials, potentially providing more targeted and efficient options for managing hyperandrogenism and insulin resistance in PCOS [43].

8.3 Research Gaps

Despite significant advancements in the study of polycystic ovary syndrome (PCOS), several research gaps persist that require further investigation. There is a pressing need for longitudinal studies to comprehensively understand the long-term reproductive, metabolic, and cardiovascular outcomes in women with PCOS, including how the syndrome affects menopause and post-menopausal health. Current research often focuses on specific populations, neglecting the inclusion of diverse ethnic and racial groups, which is crucial for understanding the varied manifestations and impacts of PCOS across different backgrounds. Additionally, while the link between PCOS and infertility is well-established, the precise mechanisms by which PCOS disrupts fertility remain unclear, necessitating further exploration to enhance fertility treatments. The influence of environmental factors, such as endocrine-disrupting chemicals and lifestyle choices, on the development and progression of PCOS is another area where more research is needed. Finally, although the psychological burden associated with PCOS is increasingly recognized, there is a significant gap in the development and validation of effective

psychological and behavioural interventions to support affected individuals [3,9,14,17,37,39,40,43].

9. Conclusions

The findings of this review underscore the necessity for a multifaceted approach to the management of PCOS. Clinicians should prioritize individualized treatment strategies that address both the reproductive and metabolic aspects of the syndrome. The emphasis on emerging therapies, such as insulin sensitizers and anti-inflammatory agents, points toward a future where treatment is increasingly tailored to the specific needs of each patient. Furthermore, the recognition of the psychological burden associated with PCOS highlights the importance of integrating mental health support into routine care. Continued research into the underlying mechanisms of PCOS, as well as the development of innovative therapeutic strategies, is essential for improving patient outcomes.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT-3.5 to check spelling and grammar. After using this tool, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

Author Contributions

RSH conceptualized the study, developed the framework, and led the drafting. SBD contributed to data analysis, writing, and revising. OA contributed to the interpretation of data for this work, supervised the project, reviewed the manuscript, and ensured alignment with journal requirements. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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