# The Stolen Femininity of Patients with Polycystic Ovarian Syndrome (PCOS): Review Article

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## *Abstract*

Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age. Hormonal imbalances, especially elevated levels of male hormones (androgens), result in a range of physical manifestations and fertility issues. In particular, PCOS has a noticeable impact on physical appearance, including excessive hair growth in areas typically associated with males, acne, and oily skin; these manifestations can cause significant distress and negatively affect self-esteem and body image. Furthermore, the androgenic burden disrupts the normal menstrual cycle, leading to irregular or absent periods, and making it difficult for women with PCOS to conceive naturally. Understanding the wide range of manifestations of PCOS and its effect on women is crucial as they can challenge their self-image and societal perceptions of femininity. Therefore, understanding these issues is important for developing effective interventions to address the physical and psychological consequences of this condition, thereby improving the quality of life of affected women.

**Keywords:** Polycystic Ovary Syndrome, Physiopathology; Women health; Infertility; Management.

## Introduction

Polycystic ovarian syndrome (PCOS) is a multifactorial endocrine disorder caused by an imbalance of androgens (male hormones).[1] It affects approximately everyone in 5 to 10 women of reproductive age, usually manifesting in adolescence.[2,3] However, the exact global burden of the condition remains unknown, as up to 70% of cases are estimated to go undiagnosed.[4] To date, PCOS is one of the leading causes of female infertility.[5] This review delves into the pathophysiology, physical and psychological manifestations, and management of PCOS. In particular, the article emphasizes the importance of patient education focusing on the short- and long-term consequences of PCOS, as well as the importance of routine screening to address the psychological dimensions of this condition in order to facilitate effective lifestyle changes and support the overall wellbeing of affected individuals.

## *Pathophysiology*

Although distinguishable from other ovarian conditions by internal ovarian causes, external ovarian factors including hyperinsulinemia, and the abnormal production of ovarian and/or adrenal androgen, the precise etiology of PCOS remains unknown.[6] The normal activity of the ovaries is disturbed by insulin resistance, which raises androgen levels and causes anovulation; furthermore, levels of other hormones are also abnormal, including prolactin, luteinizing hormone, follicle-stimulating hormone, and gonadotropin-releasing hormone.[7,8] While the precise processes governing its heritability remain unknown, PCOS is assumed to have a complex pathophysiology, influenced by the

susceptibility of individuals with predisposing genetic features to potent environmental stimuli, such as poor diet, lifestyle, or exposure to infectious agents.[9,10]

Genetic factors play a significant role, although pinpointing the exact underpinnings of the condition is challenging due to unreliable investigative measures and the heterogeneous clinical manifestations of PCOS, even within members of the same family.[6] Nonetheless, familial aggregation is evident. For example, one study found that the daughters of mothers with PCOS have a five-fold increased chance of developing the condition compared to those whose mothers do not have the condition.[11] Another indicated that a woman has a 50% chance of acquiring PCOS if her mother or sibling also has the condition.[12]

Propensity to PCOS may be influenced by various genes that regulate gonadotropin secretion, ovarian function, and hormone action, including follicle-stimulating hormone beta-polypeptide (FSHB), luteinizing hormone/choriogonadotropin receptor (LHCGR), follicle-stimulating hormone receptor (FSHR), anti-Müllerian hormone (AMH), and differentially expressed in normal and neoplastic cells domain containing 1A (DENND1A). Genome-wide association studies have also identified associations with candidate metabolic genes like thyroid adenoma-associated gene (THADA) and insulin receptor (INSR) gene.[13,14] There is also a notable link between PCOS and hyperinsulinemia, potentially resulting from two primary factors: an increase in hyperandrogenism and a reduction in the levels of sex hormone-binding globulin present in the bloodstream.[15] Peripheral insulin resistance, associated with uterine and ovarian problems, also has a genetic basis.[16] Both the male and female offspring of women with PCOS are more likely to become insulin-resistant compared to those born to women without PCOS.[17,18]

Neurokinin B (NKB) is a hypothalamic neuropeptide that plays a significant role in the regulation of gonadotropin-releasing hormone (GnRH) secretion, which is central to the control of the menstrual cycle and ovulation. In PCOS, an imbalance in the hormonal feedback system often results in reproductive dysfunction, including irregular menstrual cycles and anovulation.[19]

Kit ligand (KL), also known as stem cell factor (SCF), is a an intraovarian cytokine that plays a crucial role in folliculogenesis, the process by which ovarian follicles mature. KL interacts with its receptor, Kit, which is expressed on various ovarian cells, including granulosa cells and thecal cells. KL signaling promotes the growth and development of oocytes and granulosa cells and is essential for proper follicle maturation. Dysregulation of KL signaling has been implicated in the pathophysiology of PCOS. The interplay of increased NKB levels and KL signaling provides insight into the complex and multifaceted nature of PCOS. Both mechanisms impact key processes involved in reproductive function.[20]

Lifestyle factors also influence the development of PCOS, particularly a poor diet, a factor which heightens the risk of metabolic disease.[16]m Weight gain and obesity contribute to PCOS through metabolic and hormonal effects associated with insulin resistance and hyperinsulinemia.[21] Exogenous toxins accumulating in the follicular environment due to specific lifestyle choices, such as a diet rich in advanced glycation end-products and exposure to endocrine-disrupting chemicals, may also influence PCOS development.[22] Chronic stress exacerbates the condition by triggering adipocyte hypertrophy and activating the hypothalamic-pituitary-adrenal (HPA) axis, leading to cortisol release. This promotes gluconeogenesis, lipolysis, visceral fat accumulation, and increased insulin levels, primarily through the effects of glucocorticoids on pre-adipocyte formation.[23] While studies have associated PCOS with specific dietary components like saturated fatty acids and vitamin D deficiency, the exact role of nutrition remains unclear.[24] Prenatal exposure to the highly androgen-concentrated intrauterine environments of mothers with PCOS is also considered a contributing environmental factor.[25]m

## *Physical and Psychological Manifestations*

As mentioned previously, women with PCOS exhibit a wide range of physical symptoms, including amenorrhea, oligomenorrhea, hirsutism, weight gain or obesity, anovulation, androgenic alopecia, acanthosis nigricans, and acne vulgaris.[1,26] In addition, PCOS is associated with adverse reproductive (menstrual irregularity, subfertility or infertility), metabolic (insulin resistance, diabetes mellitus, cardiovascular risk), and psychological (anxiety, depression, personality disorders) complications.[27]

In PCOS, the usual hormonal balance in the body is disrupted. Elevated androgen levels and the development of small fluid-filled cysts in the ovaries inhibit folliculogenesis and the development, maturation, and release of eggs; this can lead to missed or infrequent ovulation and subsequent menstruation, contributing to fertility problems.[28] Insulin resistance is also a common feature of PCOS, resulting in increased hunger and weight gain, especially around the abdomen.[29] The comorbid presence of metabolic conditions like insulin resistance and obesity worsen existing PCOS symptoms by further disrupting the hormone balance. Increased androgen levels can also lead to hirsutism, resulting in excessive male-pattern hair growth on the face, chest, back, and other areas; male-pattern hair loss on the scalp may also occur.[30] Finally, elevated androgen levels stimulate the sebaceous glands in the skin to produce more sebum, clogging pores and contributing to excessive oiliness and the development of acne, particularly on the face, chest, and back.[31]

his review article not only delves into the clinical and pathophysiological aspects of polycystic ovarian syndrome (PCOS) but also emphasizes the significant psychological impact the condition has on affected individuals. By examining recent study findings, we explore the emotional challenges faced by women with PCOS, including issues related to body image, self-esteem, and mental health. Furthermore, the article highlights the unique challenges of subfertility experienced by women in Arab and Asian populations, where cultural and societal factors may exacerbate the psychological burden of the condition. This comprehensive approach aims to provide a holistic understanding of PCOS, considering both its medical and psychosocial dimensions.

Several recent systematic reviews and meta-analyses have indicated that PCOS triggers emotional distress.[32] In particular, findings from one systematic review unequivocally suggested that PCOS was an independent predictor for the increased risk of psychological disorders.[33] Two studies from India found a prevalence of 28% and 39% for anxiety and 11% and 25% for depression among women with PCOS.[34,35] In the Middle East, case-control studies conducted in Saudia Arabia indicated that women with PCOS suffered more frequently from stress, depression, and anxiety compared to healthy controls.[36,37] Another study performed in Oman similarly found that the presence of PCOS was associated with greater psychological burden, as determined by an increased risk of depression, anxiety, and stress.[38]

The occurrence of psychological distress in PCOS has its roots in several important factors, including changes in appearance and self-esteem, irregular or absent menstrual periods, disturbances in sexual attitudes and behavior, hormonal fluctuations, and increased stress as a result of the challenges of living with the condition.[39] Qualitative research originating from Iran indicated that PCOS had a considerable impact on the health-related quality of life (QOL) and self-image of young women, especially when it comes to feelings of inferiority surrounding traditional concepts of femininity and fertility, concern over future marriage prospects, and loss of physical beauty or attractiveness.[40,41] In Oman, a qualitative study found that PCOS-related infertility was tied to feelings of loneliness, jealousy, and inferiority among affected women and often resulted in marital conflict and poor social relationships with family and friends due to the high degree of cultural importance placed on childbearing.[42]

One study from South India determined that psychological distress was significantly related to certain physical manifestations of PCOS, including obesity, infertility, acne, and hirsutism.[43] On the other hand, another study assessed the impact of four symptoms on depression, namely, obesity, acne, hirsutism, and acanthosis, and found no significant association between these variables.[44] This stark discrepancy in findings likely indicates that interactions between psychological distress and physical PCOS symptoms, environment, lifestyle, and hormone levels are highly complex and individualized.

To date, the exact reason for the marked vulnerability to psychiatric disorders seen in patients with PCOS remains unclear.[45] One potential cause could be stress response mediated by abnormal HPA axis activity and circadian patterns.[46] Regardless, the risk of adverse psychological consequences highlights the need for routine screening for anxiety and depressive symptoms among patients with PCOS.[47] Several studies have also suggested that the chronic, complex, and often frustrating nature of PCOS may lead to decreased motivation and confidence in affected women; as such, these dimensions should be considered essential focuses for treatment and lifestyle modification interventions in order to improve patients' overall wellbeing and QOL.[48]

## *Spotlight on Infertility*

The prevalence of infertility in women with PCOS varies worldwide. According to a retrospective cohort study from the UK, 66% of women with PCOS are infertile, including 17.5% with primary infertility.[49] A recent systematic review estimated the overall prevalence of infertility in the Middle East and North Africa to be 22.6%, although there is no published information concerning the prevalence specifically among women with PCOS.[50] Regardless of underlying cause, infertility exacts a significant emotional toll on affected couples, notably women, irrespective of whether the condition stems from male- or female-related factors.[51] Research shows that women experiencing infertility are twice as likely to report depressive symptoms compared to those without fertility problems; moreover, infertility has been linked to lower self-perceived attractiveness and memory/concentration scores, as well as significant impairments in QOL.[52] Some researchers have posited that psychosocial distress may be a cause, rather than a consequence, of infertility.[51,53]

Efforts to understand the psychological implications of infertility among women with PCOS have yielded conflicting outcomes, with studies evaluating the QOL and psychosocial wellbeing of patients with PCOS showing varying impacts on infertility-related concerns.[54,55] While many expressed apprehension about future childlessness, infertility did not emerge as the sole determinant of psychological distress among these women.[39,56] Studies comparing PCOS-afflicted women to those experiencing infertility for other reasons found that primary causes of increased depression and body dissatisfaction in the former group stemmed more from PCOS-associated symptoms and body image issues than infertility itself.[55,57] In particular, women with PCOS have reported challenges perceiving themselves as "feminine", in part because subfertility and childlessness is seen to invalidate traditional gender roles.[54] In addition, many women with PCOS report feeling "freakish", "abnormal", and like "improper women" due to male-like symptoms (i.e., hirsutism, androgenic alopecia, etc.).[58]

Nonetheless, it should be noted that the psychosocial experience of infertility is highly related to sociocultural context.[51] For example, a study of Austrian and Muslim immigrant women found that the latter group reported considerably greater psychological distress as a result of their infertility.[59] Similarly, qualitative studies from the Middle East and Iran have highlighted the profound emotional impact of infertility among women with PCOS, with cultural expectations related to childbearing, marital pressure, and self-perception majorly contributing to psychological distress in these women.[42,58] Such variations emphasize the need for healthcare providers to consider ethnic, religious, and cultural differences when addressing the psychological implications of PCOS-associated infertility, underlining the need for a comprehensive, culturally sensitive approach in addressing these concerns.

## *Management*

The management of PCOS relies heavily on individualized approaches. Because women with PCOS exhibit such a wide and varied range of complications—including fertility concerns, menstrual irregularities, and symptoms associated with hyperandrogenism (e.g., acne, hirsutism, or androgenic alopecia)—tailored management strategies are essential to achieve optimal outcomes and meet the unique needs of each patient.[60,61] Moreover, acknowledging the psychological aspects of PCOS is crucial for facilitating lifestyle changes; as such, addressing patient education and psychosocial issues is a prerequisite for successful intervention.[62]

Initial steps in PCOS management often involve lifestyle changes, primarily weight reduction and controlling calorie intake.[63] Studies highlight that even a modest weight loss of 5% to 10% can restore regular menstrual cycles and reduce free testosterone levels, thereby decreasing the incidence of metabolic syndrome.[64] Tailored dietary plans, rich in fiber and low in saturated fats and carbohydrates, are generally recommended.[65,66] Physical activity is also significant for weight reduction and improved insulin sensitivity.[67] Exercise, regardless of dietary changes, has shown potential to restore ovulation in women with PCOS through modulation of the hypothalamic-pituitary-gonadal axis.[68]

Irrespective of weight and specific complaints, lifestyle modification is the first course of action for most patients with PCOS, particularly in mild to moderate cases.[47] However, pharmacological interventions might be necessary in some cases. For women primarily concerned with menstrual irregularities who are not seeking to become pregnant, combined oral contraceptives (COCs) or progestins are frequently recommended.[69] Metformin, with its insulin sensitivity-enhancing properties, is often prescribed alongside COCs to restore ovulation in patients with PCOS; this

drug also shows short-term anti-hyperandrogenic effects.[70] Patients seeking relief from hyperandrogenism-related dermatological manifestations may benefit from aldosterone receptor antagonists or 5-alpha reductase inhibitors.[71] Treatment strategies vary for patients experiencing infertility, where medications for ovulation induction such as clomiphene citrate and aromatase inhibitors become pivotal.[72,73]

Healthcare providers should be trained to understand and respect the cultural nuances that affect how women in specific regions view PCOS and fertility. For instance, in many Arab and Asian cultures, the emphasis on family and having children may intensify feelings of inadequacy or failure among women experiencing subfertility. Sensitively addressing these concerns, and providing psychological support along with fertility treatments can improve the overall care experience. Moreover, Increasing awareness and education about PCOS, particularly its psychological impact, through community outreach programs or mass media campaigns can help reduce stigma and misconceptions. Educating affected women, families and partners about PCOS can also alleviate the social pressure on women who may face judgment or misunderstanding about their condition.

## Conclusion

Addressing PCOS poses a significant challenge due to its multifaceted nature and complex pathophysiology. The broad range of physical symptoms in PCOS profoundly impacts the QOL of affected individuals; in addition, psychological repercussions, notably a heightened risk of anxiety, depression, and stress, are critical considerations. Women with PCOS face unique challenges, encompassing concerns about appearance, gender identity, and sociocultural pressures, emphasizing the need for holistic care that addresses the complex interplay between medical and psychosocial aspects. Infertility, a significant outcome of PCOS, may intensify emotional distress and cultural sensitivity is key in addressing these concerns. Comprehensive care for PCOS demands a holistic approach, integrating lifestyle modification and pharmacological intervention with psychological support and patient education.

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