Rethinking the Terminology: A Perspective on Renaming Polycystic Ovary Syndrome for an Enhanced Pathophysiological Understanding

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ABSTRACT: Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder that affects women at various stages of life, presenting a wide range of symptoms and health implications. The term "Polycystic Ovary Syndrome" can be misleading, prompting many within the medical community and advocacy groups to advocate for a name change. Critics argue that this terminology can complicate understanding and awareness of the disease among patients. The primary concern is that PCOS emphasizes the ovarian aspect, fostering the misconception that PCOS is merely a gynecological disorder. In reality, PCOS impacts multiple organ systems, particularly metabolic health. Patients frequently experience insulin resistance, weight gain, irregular menstrual cycles, and hirsutism—symptoms that extend beyond ovarian dysfunction. In light of these issues, there is increasing support for renaming PCOS to better reflect its systemic implications and minimize confusion. The current name may hinder understanding and potentially lead to inadequate disease management. Alternative names have been proposed, including "Ovarian Dysmetabolic Syndrome," which our team supports, as well as "Metabolic Reproductive Syndrome" and "Hyperandrogenic Persistent Ovulatory Dysfunction Syndrome." These alternatives aim to highlight the hormonal imbalances and metabolic disturbances associated with the condition, fostering inclusivity and reducing stigma for all affected individuals. This narrative review provides a historical overview of PCOS, tracing its recognition from early descriptions to contemporary guidelines. We discuss the evolving understanding of its pathophysiology and the rationale behind the proposed name change. By adopting a new nomenclature, we can enhance understanding among healthcare professionals, increase inclusivity for affected women, reduce the stigma and anxiety linked to the diagnosis, and offer a more accurate representation of the condition's complex pathophysiology.

PLAIN LANGUAGE SUMMARY

Changing the name "Polycystic Ovary Syndrome" to better reflect the underlying biological mechanisms of the condition

Polycystic Ovary Syndrome (PCOS) is a complicated hormone disorder that causes a variety of symptoms and health problems. However, the name "Polycystic Ovary Syndrome" has been criticized by doctors and advocacy groups for being misleading. They argue that the name focuses too much on the ovaries, which might make people think PCOS is only a gynecological issue. The main reason for considering a name change is to better represent the full range of health issues associated with PCOS. For example, "Hyperandrogenic Anovulation" or "Metabolic Reproductive Syndrome" have been suggested as new names. These alternatives aim to highlight the hormonal and metabolic aspects of PCOS, helping to reduce stigma and making the condition easier to understand for everyone affected. In this review, we look at the history of PCOS, how our understanding of its causes has changed over time, and the reasons for wanting to change its name. We also discuss different new names that have been suggested. Changing the name could help doctors and patients better understand the condition and make it more inclusive for all women who have it.

KEYWORDS: Polycystic ovary syndrome, metabolism, hyperandrogenism, obesity, type 2 diabetes, dysmetabolism

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Introduction

Polycystic Ovary Syndrome (PCOS) is an endocrinopathy primarily affecting women of reproductive age.[1] Over time, it has become the most common endocrinopathy among post pubertal women, with a prevalence of approximately 10% to 20% worldwide.[2] Since its initial scientific description by Stein and Leventhal in 1935, the syndrome has gained popularity and increased in incidence, especially after the publication of its first international recommendations in 2003.[3]

PCOS is characterized by hyperandrogenism, chronic anovulation, and a polycystic morphology of the ovaries. The clinical presentation of PCOS is quite heterogeneous; with hirsutism, menstrual irregularities, and infertility being the most common manifestations.[4] These women also have a higher prevalence of obesity, metabolic disorders, and an increased risk of diabetes, hypertension, and dyslipidemia.[5] Despite an uncertain etiology, current data suggest that complex interactions between genetic, environmental, and behavioral factors contribute to the heterogeneous clinical

expression of PCOS.[6] This pathophysiology is becoming more and more complex as new factors are emerging from the ongoing research.

The management of PCOS is highly variable, and the literature confirms the challenges that healthcare professionals, regardless of their specialty, are facing to properly manage this syndrome.[7] In fact, given the significant variability in clinical and biological symptoms associated with PCOS, the management can be led by various specialists, including endocrinologists, gynecologists, dermatologists or psychiatrists. Regardless of the chosen approach, there is a fundamental need for multidisciplinary care to address the spectrum of potential complications throughout the patient's life.

One major reason for mismanagement by healthcare professionals is the complexity of PCOS pathophysiology. Naming the disease "polycystic ovary syndrome" leads most of the clinicians to think of a gynecological disorder.[8] Even patients who identify themselves as having PCOS often naturally assume that the problem stems solely from the ovaries.[9] While the ovaries play a crucial role in this pathophysiology, the issue is much deeper than just the polycystic aspect of the ovaries.

In light of this observation, many voices have advocated for changing the name of the disease, which can mislead patients or healthcare professionals into considering this condition solely from a gynecological perspective.[10,11] Indeed, the disease's current name does not highlight hyperandrogenism, a major symptom of the condition, or the metabolic component that explains a significant portion of its pathophysiology. This is particularly noteworthy because many other endocrinopathies or metabolic disorders include terms in their names that reflect the fundamental pathophysiology of the disease, such as the recent change from Non-Alcoholic Steatohepatitis to Metabolic Dysfunction-Associated Steatohepatitis.[12]

The urgency of renaming PCOS is crucial given the high prevalence and complexity of the disease to improve its management and terminology.

In this narrative review, we will explore the historical foundations of the disease, provide a summary of PCOS history and pathophysiology, and conduct a descriptive analysis of the new nomenclatures proposed in the literature, including our own proposition in this regard.

Brief Methodology

In this, we performed a narrative review to explore the historical evolution and proposed name changes for PCOS. To ensure a comprehensive overview, we searched the following databases: PubMed, NCBI, Embase, and Cochrane Library. Our search included publications from the earliest available records up to the present. We used search terms such as "Polycystic Ovary Syndrome," "Polycystic Ovary Disease," "PCOS diagnosis," "PCOS treatment," "PCOS pathophysiology," "Ovarian dysfunction," "Ovarian dysmetabolic syndrome," "Metabolic reproductive syndrome," "Hyperandrogenic Persistent Ovulatory Dysfunction Syndrome," "Insulin resistance in PCOS," "Hyperandrogenism," "Metabolic syndrome and PCOS," "PCOS and cardiovascular risk," "PCOS and infertility," "PCOS and obesity," "PCOS and diabetes," "Endocrine dysfunction in PCOS," "PCOS and hormonal imbalance," "PCOS metabolic complications," "PCOS and reproductive health," "History of PCOS," "Renaming PCOS," "PCOS and ovulatory dysfunction," "Androgen excess in women," "PCOS-related infertility," "PCOS guidelines," "PCOS research," "Hyperinsulinemia in PCOS," "PCOS clinical manifestations," "PCOS in adolescence," "PCOS long-term health risks."

We focused on original research articles, comprehensive reviews, and key guideline documents that addressed the development of PCOS nomenclature, its metabolic and reproductive implications, and the rationale for proposed changes in terminology. Articles were selected based on their relevance to the pathophysiology of PCOS, with particular attention given to those that marked significant turning points in understanding the syndrome's systemic nature.

Inclusion criteria for article selection comprised: (1) peer-reviewed articles published in English or French; (2) research specifically focused on PCOS or its proposed alternative nomenclature; (3) studies providing clinical, epidemiological, or genetic insights related to the condition; and (4) relevant guidelines or consensus statements.

Exclusion criteria included: (1) non-primary research articles; (2) studies focusing on non-human subjects; (3) works that lacked relevance to the review objectives; and (4) articles published before a specified cutoff date that were deemed not significant for current understanding.

Priority was given to high-impact studies that contributed to the ongoing discussion surrounding the renaming of PCOS, ensuring the review's findings are grounded in robust, scientifically credible literature.

History of PCOS

The first scientifically documented description of PCOS was provided by Stein and Leventhal,[13] 2 American gynecologists who observed the presence of common symptoms in a number of patients, including infertility and polycystic ovaries.

However, some articles revealed that the initial observation may have been made by an Italian scientist named Vallisneri in 1721, who described the ovaries of a married, infertile woman as shiny, having a white surface, and as big as a pigeon's egg.[14] Another notable account was made in 1844 by Chereau and Rokitansky who described fibrous and sclerotic lesions in ovaries of a degenerative character with hydrops follicle.[15] In 1879, Lawson Tait advocated for bilateral oophorectomy as a treatment for symptomatic cystic degeneration of the ovaries. Partial resection of the ovaries was subsequently proposed.[14] In 1902, von Kahlden published a review on the pathology and clinical implications of these ovarian conditions.

Over the years, and with advancements in hormonal and gynecological investigations, subsequent descriptions have primarily focused on adding isolated descriptions of each

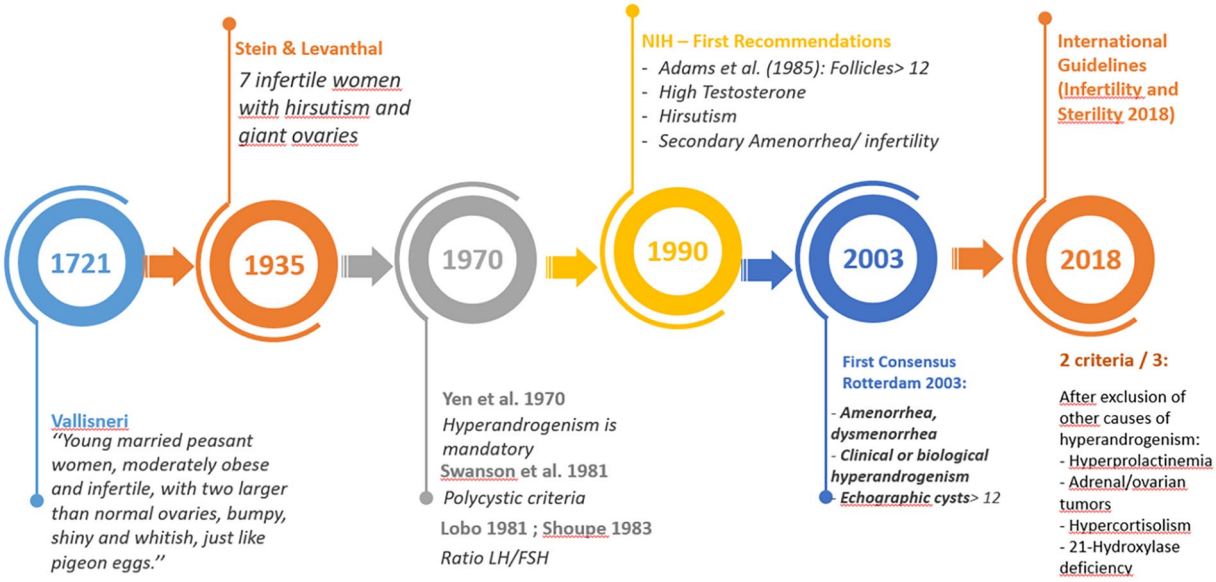

Figure 1. Summary of the major historical milestones in natural history of polycystic ovary syndrome.

preceding symptom (Figure 1). In 1958, three investigators were the first to describe an increased level of luteinizing hormone (LH) in women with bilateral cystic ovaries.[16] This increase of the LH, alongside with an increase of testosterone were considered to be crucial for diagnosing PCOS. Following this statement, Yen et al[17] defined hyperandrogenism as a fundamental criterion of the syndrome, Swanson et al[18] emphasized the polycystic criterion, and, in the eighties, was introduced the concept of an inverted follicle stimulating hormone (FSH) on LH ratio.[19]

In 1985, Franks et al[20] discussed the threshold of 12 follicles per ovary as the pathological limit for an ultrasound-diagnosed polycystic ovary. It was only in 1990 that the first premises of guidelines, combining criteria for the syndrome, began. The criteria discussed in this context were ultrasound-diagnosed polycystic ovaries, infertility, and hirsutism. The initial official designation for these criteria was known as the "NIH Criteria."[21]

The first consensus was not established until 2004. The 2004 criteria, set forth by a group of experts during a conference in Rotterdam, the Netherlands, held in 2003, are considered standard (The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group).[22] The Rotterdam definition is broader and includes a larger number of patients, particularly those without clinical or biochemical hyperandrogenism, whereas the NIH definition required biochemical hyperandrogenemia for diagnosing PCOS. Critics of the Rotterdam criteria argue that they encompass milder phenotypes, especially those involving the combination of polycystic ovaries with oligomenorrhea. They also believe that results obtained from studies on patients with excess androgens may not be applicable to normoandrogenic patients and may also inflate the prevalence of PCOS in the general population.

In 2006, the Androgen Excess Society made an attempt to establish hyperandrogenism as a necessary diagnostic condition when combined with other signs of the syndrome.[23] The emphasis on hyperandrogenism aimed to exclude milder phenotypes and was based on evidence indicating that hyperandrogenism often correlates with both reproductive and metabolic symptoms of the syndrome.

Subsequently, the criteria have become increasingly refined through the 2018 recommendations and, most recently, in 2023 individualizing multiple phenotypes through evolutions of Guidelines (Table 1).[24,25] These updates have primarily improved diagnostic criteria by adding information about anti-Müllerian hormone (AMH), the significance of dehydroepiandrosterone sulfate (DHEA-S), and most importantly, shedding light on the numerous hidden complications of PCOS, particularly psychiatric ones.

Also, recent advances in the understanding of PCOS highlight the significant role of genetics and environmental factors in its pathogenesis. Genome-wide association studies (GWAS) have identified multiple genetic loci linked to the syndrome, particularly those involved in metabolic and reproductive pathways.[7] These findings support the idea that PCOS is a complex genetic condition rather than a disorder caused by a single gene. In addition to genetic factors, the role of insulin resistance and hyperandrogenism is being further explored through these studies, contributing to a more precise understanding of its phenotypes.

Environmental influences also play a key role in the development of PCOS. Exposure to endocrine-disrupting chemicals, early-life nutrition, obesity, and stress have been associated with an increased risk of developing the syndrome.[6] These factors suggest that PCOS may have its origins in early life, with fetal exposure to certain environmental elements predisposing individuals to the condition. Understanding these environmental contributions offers new perspectives on both the diagnosis and management of PCOS, reinforcing the call for renaming the condition to better reflect its complex etiology.

Table 1. PCOS phenotypes through the evolution of diagnostic criteria.

		PCOS PHENOTYPES			
		A	B	C	D
Features					
	Hyperandrogenism/ Hirsutism	X	X	X	
	Ovulatory dysfunction	X	X		X
	Echographic polycystic ovaries	X		X	X
Diagnostic criteria					
	NIH 1990	X	X		
	AE-PCOS society	X	X	X	
	Rotterdam 2003	X	X	X	X
	2018/2023 guidelines	X	X	X	X

Main Pillars in the Pathophysiology of PCOS

The main cause of difficulties in understanding the pathophysiology of PCOS is its heterogeneous and complex nature. If we were to focus solely on the diagnostic triad of hyperandrogenism, menstrual irregularities, and ultrasound polycystic morphology, we would still have limited understanding of the underlying processes that have led to these symptoms.

Hyperandrogenism, ovulatory dysfunction, abnormal gonadotropin-releasing hormone (GnRH) pulses, and the subsequent irregular gonadotropin secretion, along with insulin resistance, have all been implicated in the pathophysiology of PCOS (Figure 2).[6,26] These factors interact with and exacerbate each other in the development and progression of the syndrome.

Genetic predisposition

Initially, the main aim was to find a single candidate gene to identify the transmission of the disease.[27] However, this research proved futile because there was no single gene responsible for the condition.[28] Instead, PCOS is characterized by polygenic transmission, similar to other metabolic disorders.[29] Limited number of genes have been connected with PCOS through chronic inflammation, steroid hormone actions, energy homeostasis, insulin action, insulin secretion, gonadotrophin regulation and action, ovarian and adrenal steroidogenesis.[30] The strongest associated genes with PCOS are FTO, AR, CAPN10, CYP450, INS, and FSHR.[31] The genetic susceptibility to PCOS varies among individuals within the same family.[32] Recently, intrauterine programing has been proposed as a susceptibility factor for PCOS.[33] Parental analysis is often impractical in diseases like PCOS; however, the known risk of the disease can be estimated through other means.[34]

Ovarian and adrenal hyperandrogenism

There is substantial evidence suggesting that PCOS is an intrinsic disorder of the ovaries, and the primary defect lies in the increased biosynthesis of androgens.[35] Typically, ovarian theca cells produce androgens in response to LH. These theca cells express the CYP17A1 gene, which encodes the P450c17 enzyme responsible for both 17α-hydroxylase and 17,20-lyase activities, which are the rate-limiting steps in sex steroid synthesis.[36] Androgen production follows a cyclical pattern and is regulated by both intra-ovarian and extra-ovarian mechanisms.[37] As LH levels increase, there is a downregulation of LH receptors and a decrease in CYP17A1 expression, leading to a reduction in androgen production. Estrogen and androgen act in a negative feedback loop to inhibit 17α-hydroxylase and 17,20-lyase activity in a paracrine and autocrine manner.[38] In contrast, insulin stimulate the P450c17 enzyme and up-regulate LH receptor sites.[39] This can further contribute to the overproduction of androgens in individuals with PCOS.

Increased adrenal DHEA-S has been suggested in PCOS women with adrenal hyperandrogenism. This adrenal hyperandrogenism does not appear to be dependent on an increased hypothalamic-pituitary-adrenal drive. Instead, it reflects a generalized adrenal hyper-responsiveness in terms of androgenic biosynthesis. Since the 2018 recommendations, further supported by those in 2023, measuring serum DHEA-S has become necessary when testosterone levels are within the normal range.[25] This emphasizes the importance of adrenal function and its secretory abnormalities, which are responsible for hyperandrogenism in approximately 45% of cases in PCOS.

Insulin secretion and insulin resistance

Insulin is indeed the sole hypoglycemic hormone in the organism. Its decrease is indicative of diabetes mellitus, with the primary etiology being type 2 diabetes (T2D), caused mainly by insulin resistance. Clinical studies, supported by genetics, confirm an overlap in both the transmission of genes related to T2D and PCOS, and in the transmission of insulin resistance genes and PCOS.[40] Insulin resistance is also exacerbated by irregular dietary habits that promote obesity, as well as by a chronic stress inducing environments (pseudo-Cushing).[41] Enhanced insulin secretion directly induces the pituitary gland to release LH, which subsequently initiates the secretion of androgens and influences the maturation and growth of ovarian follicles.[42] Elevated levels of insulin and androgens collectively impede the production of sex hormone-binding globulin (SHBG), leading to an elevation in the levels of free and bioactive androgens.

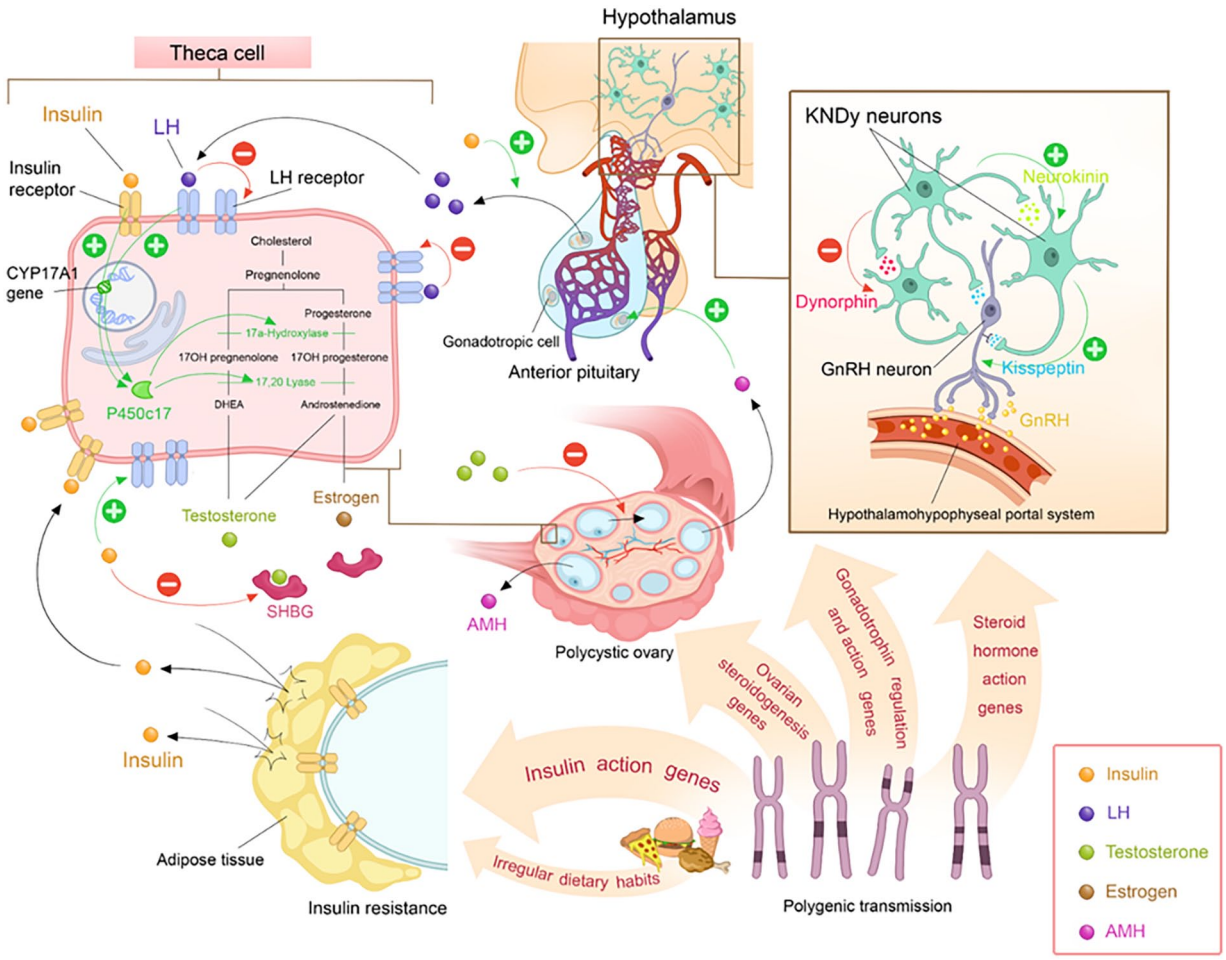

Figure 2. Main features explaining the Pathophysiology of polycystic ovary syndrome (PCOS).
Hyperandrogenism is a key feature and has a synergistic effect with insulin resistance to induce the development of PCOS. The hypersecretion of androgens is caused by intrinsic dysfunction of theca cells and/or the hypothalamus-pituitary-ovarian axis, while hyperandrogenism causes abnormal GnRH pulsation and gonadotropin secretion through the aberrant negative or positive feedback of estrogen. Both kisspeptin neuron and KNDy neuron can generate and release kisspeptin, which binds with the receptors expressed by GnRH neuron, facilitating the release of GnRH. Therefore, over-expressed kisspeptin leads to a higher LH pulses and excessive androgen secretion, which disturbs the function and morphology of ovary. The abnormal gonadotropin secretion in patients with PCOS is characterized by a high LH/FSH ratio, which induces ovarian dysfunction, including the hypersecretion of androgens. LH stimulates the classical pathway of androgen synthesis in ovarian theca cells. Cholesterol is transported to the inner mitochondrial membrane. A cleavage system of the cytochrome P450 enzyme, converts cholesterol to pregnenolone. Pregnenolone is transported to smooth endoplasmic reticulum where it is converted to 17-hydroxypregnenolone and subsequently to dehydroepiandrosterone by the 17-hydroxylase and 17,20-lyase subunit of the CYP17A1 enzyme, respectively. Dehydroepiandrosterone is then converted to androstenedione or androstenediol and subsequently to testosterone. Androstenedione and testosterone diffuse into granulosa cells where they are converted to estrogens by the action of aromatase, under the control of FSH. In addition, the high concentration of anti-Müllerian hormone (AMH), which is secreted by the antral follicles that accumulate in the ovaries of women with PCOS, further exacerbates the ovarian dysfunction by having deleterious effects on the follicular microenvironment and/or LH pulsation. Hyperandrogenism is further aggravated by hyperinsulinemia, which develops secondary to insulin resistance. Hyperinsulinemia causes an increase in androgen secretion by theca cells and an inhibition of the production of sex hormone-binding globulin (SHBG) in the liver, thereby increasing the circulating concentration of bioactive free testosterone. Insulin resistance develops in tissues and is associated with adipocyte dysfunction.

Anti-mullerian hormone

Women diagnosed with PCOS exhibit higher levels of AMH compared to those without the condition. This suggests the potential use of AMH as a surrogate marker for diagnosing PCOS. The elevation of AMH levels is driven by an increase in the number of preantral and small antral follicles.[43] This is typically observed in conjunction with anovulation. It is important to note that an increased number of small follicles does not preclude the possibility of anovulation; rather, it is a common feature of the condition. The presence of a high number of small follicles reflects disrupted follicular development and maturation, which often results in the failure to ovulate. Therefore, while an increased follicle count is indicative of PCOS, it can coexist with anovulation due to the impaired hormonal regulation and follicular growth dynamics typical of the syndrome.

However, the rise in AMH levels cannot be solely attributed to the increased follicle count. Elevated AMH levels have been observed in both anovulatory and normal-ovulatory PCOS cases when compared to non-PCOS cases.[44] Although the exact reasons for the excessive production of AMH remain unclear, a positive correlation has been established between androgens and AMH expression.

Normal AMH levels can be observed in patients with normal follicle counts, particularly in those with the type B phenotype of PCOS. This phenotype is characterized by a lower number of follicles and less pronounced hyperandrogenism.

Therefore, while elevated AMH levels are commonly associated with increased small follicle counts, normal AMH levels may still occur when follicle counts are within the normal range.

The role of AMH in the diagnosis of PCOS has been supported in the latest recommendations from 2023. However, it is emphasized that AMH should not be used in adolescents due to the potential false-positive results.[25]

Neuroendocrine alterations

Given that hyperandrogenism is a prominent feature of PCOS, substantial attention has been directed toward investigating potential mechanisms by which dysregulated androgen secretion contributes to the neuroendocrine changes seen in the syndrome. There is compelling evidence to suggest that elevated androgens disrupt the ability of sex steroids to regulate the secretion of GnRH and LH through classical feedback mechanisms.[45] This disruption leads to reduced negative feedback effects of ovarian steroids, hence the sustained excessive LH secretion characteristic of PCOS.

Among the various types of neurons that send signals to GnRH neurons, Kiss1 neurons, which produce kisspeptins (encoded by the KISS1 gene), have gained attention in the last decade as central regulators of GnRH secretion and ovulation.[46] As kisspeptin, neurokinin and Dynorphin (KNDy) neurons are sensitive to sex steroids and play a role in modulating the generation of GnRH pulses, it is reasonable to speculate that dysregulated function of this neuronal population may contribute to the neuroendocrine changes observed in PCOS.[47]

Concerning the Naming of PCOS

As one might anticipate, there have been previous efforts to rename the disorder, starting with the transition from Stein-Leventhal syndrome to PCOS (because the disorder does not seem to represent a specific disease).[11] Lobo[48] suggested changing the disorder's name to "hyperandrogenic chronic anovulation" to better reflect the underlying and often distinctive feature associated with the disorder—hyperandrogenism. More recently, Behera et al[49] proposed renaming PCOS as "estrogenic ovulatory dysfunction" or "functional female hyperandrogenism." Notably, both of these suggestions aimed to name the disorder based on general characteristics related to the condition itself, although paradoxically, they may have been considered too general to be sufficiently informative.

Many name changes have indeed been applied to various diseases or disorders, such as "mongolism" being renamed to "Down syndrome" or "manic depression" becoming "bipolar disorder." In some cases, diseases have even been named after individuals, like the change from "senile dementia" to "Alzheimer's disease." These shifts in terminology reflect evolving understanding and sensitivity in the field of medicine.

Since the 2003 guidelines, the term PCOS has been retained, making it much simpler to disseminate information about the condition and compile research under a single name, yet it is criticized mainly because it categorizes the syndrome primarily under the ovarian aspect of the condition. It focuses solely on the ultrasound description of PCOS, which gave the syndrome its name.

Why Changing the Name of PCOS is Important

Further support for a name change for PCOS stems from a study in Australia. In a cross-sectional study of 57 women with PCOS and 105 primary care physicians, 48% of the participating women agreed that the name PCOS was confusing, and 51% of them agreed that the name should be changed.[50] Among primary care physicians, 74% agreed that the name was confusing, and 81% of them agreed that it should be changed to reflect the broader clinical syndrome.[50] Moreover, to further understand the relevance of changing this syndrome, we should also note that 81% of women and 93% of primary care physicians in this study felt that an appropriate name was important for women with the condition; and 60% and 72%, respectively, felt that an accurate name would be useful for physicians.[50]

As we have seen, changing the names of diseases is a common occurrence. It's also worth noting that such changes typically happen relatively late in the course of understanding a disease, when our understanding of the condition has become comprehensive enough to focus on the simple nomenclature of the disease. The main presented argument in favor of changing the condition's name are:

The name is confusing

The example of diabetes insipidus, which historically referred to a deficiency in antidiuretic hormone, is particularly relevant. For many years, scientific societies debated the name of this condition, as it often led to confusion with diabetes mellitus among patients. In 2023, the European Society addressed this issue by renaming the condition "Arginine Vasopressin Deficiency" to clarify its nature and reduce misunderstanding.[51]

Similarly, PCOS can lead to significant confusion. On one hand, it may be perceived primarily as a gynecological disorder, prompting patients to seek care from gynecologists even if their phenotype is predominantly metabolic. On the other hand, the term's focus on ovarian cysts can overshadow the condition's broader metabolic aspects.

Moreover, the name is misleading because it implies that polycystic ovaries are a cause of the disorder, whereas they are merely associated with it. This misnomer not only complicates diagnosis and management but also contributes to the misunderstanding of PCOS's complex pathophysiology.

The name has negative associations and perceptions

An example of such a change is the transition from the terms "hermaphrodism" and "pseudohermaphrodism" to "disorders of sex differentiation".[52] The naming of these anomalies, which

often carry significant psychological burdens, has only served to reinforce the sense of disease by labeling them with caricatured mythological figures.

It's important to note that PCOS affects individuals differently, and not everyone with PCOS will experience all of these negative associations. Moreover, with proper medical care, lifestyle changes, and support, many individuals with PCOS can manage their symptoms and improve their overall well-being.[53] Early diagnosis and appropriate treatment can play a significant role in mitigating the negative effects of PCOS. Support groups and mental health resources can also help individuals cope with the emotional aspects of living with PCOS.[54]

The other misconception that can arise from the term "polycystic" is the potential error that patients may make in believing that it is associated to ovarian tumors.[55] Several authors have highlighted this mistaken perception among patients, who subsequently develop a fear of the syndrome's name.[56] Physicians should make an additional effort in this regard to explain that PCOS is characterized by the presence of small, fluid-filled sacs called cysts on the ovaries, which are actually follicles that have not developed properly. These cysts are not tumors in the traditional sense, as they are not composed of abnormal or cancerous cells. Instead, they are a normal part of the ovarian structure and can be seen in many women, even those without PCOS.

The name is simply a descriptive state

Using a purely descriptive name for a disease based on the observation of its symptoms is an ancient tradition in medicine. Among the most caricatural examples, we can mention the "mad cow disease," which is merely a description of the neurological disorders that cattle develop. Returning to "diabetes insipidus," the name was coined because the urine of patients differed from that of patients with "diabetes mellitus," hence the term "insipidus." Although the terminology is quite precise and purely descriptive, it can lead to a misunderstanding of the 2 conditions.

PCOS was initially named based on its ovarian description, as this was one of the characteristic elements that attracted gynecologists. Over time, as it became a diagnostic criterion, the terminology remained unchanged despite constant updates in recommendations. Therefore, it is a simple ultrasound description that has 2 problems in its conception: first, it is not a constant criterion, and patients without polycystic PCOS feel burdened with an additional criterion that does not apply to them.[57] Secondly, as mentioned earlier, considering the entire disease with its highly complex pathophysiology based on a simple ultrasound description, which is nothing more than the result of a multifactorial mechanism upstream, tends to obscure its understanding and contributes to the complexity of its management.

Suggested Names Instead of PCOS

PCOS does indeed have its roots in the early identification of enlarged ovaries with multiple small cysts, but as our knowledge of the condition has evolved, it's become clear that PCOS is more complex and systemic than the name might suggest.

However, it's important to note that changing the name of a well-established medical condition can be a complex process and may not necessarily lead to immediate widespread adoption. There are some challenges and considerations to keep in mind:

- Historical Recognition: The name PCOS has been in use for several decades and is recognized by healthcare providers, researchers, and patients worldwide. Changing it could lead to confusion, especially during the transition period.[58]
- Global Consistency: Medical terminology often strives for consistency and international recognition. Any name change would need to be considered on a global scale to ensure uniformity in diagnosis and treatment.[59]
- Patient and Public Awareness: PCOS advocacy groups and patient communities have worked to raise awareness of the condition under its current name.[60] Changing the name may require a concerted effort to educate the public about the new terminology.

Regardless of the name, the most important aspect is recognizing and effectively managing the condition. Healthcare providers are now more focused on addressing the metabolic and hormonal components of PCOS to provide comprehensive care that encompasses not only reproductive health but also overall well-being and long-term health outcomes.[61] This approach recognizes that PCOS affects multiple body systems and may require a holistic approach to diagnosis and treatment. As a result, some experts and healthcare organizations have advocated for more inclusive terminology that reflects the broader metabolic and hormonal aspects of PCOS.[62]

Polycystic ovary–hyperandrogenic syndrome

This proposition was suggested by Azziz.[11] While it provides more clarity on the hormonal imbalance associated with the condition, it fails to acknowledge the significant metabolic dysfunctions that are central to PCOS. By focusing primarily on ovarian and androgen-related issues, it risks continuing the outdated understanding of PCOS as primarily a reproductive disorder.

While it does introduce another criterion into the terminology and provides more information about the disease, the fact that it does not incorporate one of the fundamental concepts in pathophysiology, which is metabolism, renders this designation as obsolete in understanding the disease as was PCOS in the beginning. The author himself explains the utility of this new terminology in his manuscript but also adjusts it with another proposal that we find more appropriate: "functional metabolic-hyperandrogenic syndrome" or better still, the "metabolic hyperandrogenic syndrome."

Hyperandrogenic persistent ovulatory dysfunction syndrome (HA-PODS)

Khadilkar[10] wrote an excellent manuscript in 2016 explaining the need to change the name of PCOS. Her equally excellent article introduces a terminology she proposes: HA-PODS. This name emphasizes the hormonal imbalance (hyperandrogenism) and persistent ovulatory dysfunction, which are core features of PCOS. It offers a precise and detailed description of the syndrome, focusing on both the endocrine and reproductive dysfunctions, but may be seen as more complex or technical than other alternatives.

She explains that HA, includes either or both hirsutism and hyperandrogenemia, while POD, or Persistent Ovulatory Dysfunction, includes either or both oligo ovulation and PCO morphology. She also suggests that the syndrome should be labeled as HA-PODS+, incorporating the first letters of whichever metabolic syndrome factor is present, such as insulin resistance, obesity, diabetes mellitus, dyslipidemia, cancer, sleep apnea, cardiovascular morbidity, or hypertension.

The author conducted an excellent analysis, including a summary table that helps encapsulate her viewpoint. We strongly believe that this terminology is the most detailed in its definition of PCOS and allows for the individualization of each PCOS based on the patient's metabolic phenotype.

Nonetheless, we can identify some drawbacks in her proposal, with the primary one being the complexity of its use among both physicians and patients. While some aspects, such as hypertension or obesity, are easy to grasp, insulin resistance remains a more complex definition to apply and is not routinely used by dermatologists or gynecologists.[63] Additionally, although this terminology certainly enables more precise patient care, using different appellations for different patients could potentially create more confusion in patients' understanding.

Metabolic reproductive syndrome

This term has been introduced by Teede et al.[64] While other terminologies tend to add more diagnostic criteria to the nomenclature, the author of this suggestion includes a pathophysiological reference in the title. This attempt appears much more relevant to us than previous ones because it is simple, provides a broader overview of the disease, and, most importantly, acknowledges the metabolic dimension of the syndrome. It removes the ovarian focus and emphasizes the systemic nature of PCOS, particularly its strong association with metabolic health issues. This terminology aligns with a broader understanding of the condition's pathophysiology. In our forthcoming recommendation, we align with this terminology for its general and more relevant nature compared to the others.

The Importance to Associate the "Metabolic Aspect" When Renaming PCOS

In modern medical practice and research, PCOS is recognized as a multifaceted disorder that involves hormonal and metabolic imbalances, often extending beyond just the ovaries. While ovarian cysts can be a characteristic feature of PCOS, they are not present in all cases, and the condition's impact on an individual's overall health goes well beyond the ovaries. Metabolic dysfunctions are considered among the most important aspects of PCOS for several key reasons:

- Obesity: Many individuals with PCOS struggle with weight management, and obesity is common among those with the condition.[65] Studies reported a prevalence of obesity in PCOS reaching 80%.[66] Obesity can exacerbate insulin resistance and metabolic issues, creating a vicious cycle that further impacts overall health.
- Impact on Fertility: Insulin resistance and its associated high insulin levels can interfere with normal ovarian function, leading to irregular ovulation and fertility issues. Infertility related to obesity with PCOS reach a prevalence of 70%.[67] Managing metabolic dysfunctions, particularly insulin resistance, can improve the chances of regular menstrual cycles and ovulation, increasing the likelihood of conception for those trying to conceive.[68]
- Risk of T2D: Insulin resistance is a major risk factor for the development of type 2 diabetes. The overall prevalence of glucose intolerance in women with PCOS was 45% (35% with prediabetes and 10% with T2D).[69] Women with PCOS are at a significantly higher risk of developing diabetes later in life, especially if metabolic issues are not addressed.[70]
- Cardiovascular Health: PCOS is associated with an increased risk of cardiovascular disease, including hypertension, dyslipidemia (abnormal blood lipid levels), and atherosclerosis (narrowing of the arteries).[71] A study showed that PCOS women had higher risk of hypertension, higher mean arterial values of blood pressure and an increased pulse rate than controls.[72] PCOS women appear to have a non-dipping aspect of hypertension.[73] Insulin resistance and hormonal imbalances in PCOS can contribute to these cardiovascular risk factors.
- Long-Term Health: PCOS is not just a reproductive disorder; it can have long-term health consequences such as cancers and psychiatric diseases.[74] Managing metabolic dysfunctions can reduce the risk of developing chronic conditions like T2D, cardiovascular disease, and obesity-related complications.
- Pregnancy Complications: Women with PCOS are at an increased risk of pregnancy complications, such as gestational diabetes and preeclampsia.[75] Managing metabolic issues before and during pregnancy can help mitigate these risks.

Why "Ovarian Dysmetabolic Syndrome" is the Best Suggestion

The suggestion to rename PCOS to "Ovarian Dysmetabolic Syndrome" or "Ovarian Dysfunctions and Dysmetabolic

Syndrome" has been proposed by some experts and researchers in the field of reproductive medicine and endocrinology.[76] The proposed name change is intended to better reflect the systemic nature of the condition, emphasizing the metabolic and hormonal aspects beyond just the presence of ovarian cysts. Here are some reasons why this idea has been put forward:

- More Comprehensive Description: "Ovarian Dysmetabolic Syndrome" highlights the fact that PCOS is not solely an issue related to the ovaries but involves metabolic and hormonal dysregulation throughout the body. This more comprehensive description could lead to a better understanding of the condition among both healthcare providers and the general public.
- Reduced Confusion: The current name, can be misleading because not all individuals with PCOS have large ovarian cysts, and cysts themselves are not the primary driver of the condition. Renaming it to something that emphasizes the metabolic and hormonal aspects might reduce confusion about the nature of PCOS.
- Improved Diagnosis and Treatment: A more accurate and descriptive name might encourage earlier diagnosis and more appropriate treatment approaches that address not only reproductive issues but also metabolic and hormonal imbalances, potentially improving health outcomes for individuals with PCOS.

Including the term "dysmetabolism" in the title, emphasizes the direction that recommendations have taken since 2003, particularly those related to dietary and hygiene guidelines.[77] Previous studies have consistently demonstrated the favorable impact of lifestyle interventions on various health indicators, related to body composition, reproductive health (biochemical and clinical hyperandrogenism, menstrual patterns, ovulatory function, pregnancy, and conception), metabolic parameters (involving insulin levels, fasting glucose levels, glucose tolerance, lipid profiles, and markers for insulin resistance), and overall quality of life.[78] Furthermore, in recent guidelines, Metformin and Myo-inositol have gained significant prominence as treatments for PCOS, both in overweight individuals and in conjunction with Clomiphene Citrate in fertility management projects.[79]

Renaming PCOS to "Ovarian Dysmetabolic Syndrome" could significantly enhance clinical management by fostering a more integrated, multidisciplinary approach. The term "dysmetabolic" highlights the importance of addressing the metabolic aspects of the syndrome, encouraging endocrinologists to prioritize monitoring and early intervention for insulin resistance, obesity, and cardiovascular risks. For gynecologists, maintaining the focus on the ovaries while broadening the scope to include metabolic dysfunctions can improve the management of fertility issues and menstrual irregularities. Dermatologists could also benefit from a more collaborative approach by recognizing the link between hyperandrogenic symptoms, such as acne and hirsutism, and underlying metabolic disturbances. This shift in terminology would promote a holistic view of the condition, ensuring that treatment across all specialties is both comprehensive and personalized, ultimately improving patient outcomes.

Conclusions

The term "Polycystic Ovary Syndrome" was historically coined to describe a condition characterized by the presence of ovarian cysts. However, it has become increasingly apparent that this nomenclature can be misleading, as not all individuals with PCOS present with large ovarian cysts, and the condition often exists without them. Moreover, PCOS is a multifaceted disorder with significant metabolic implications that extend beyond the reproductive system.

In light of the evolving understanding of PCOS, the proposed term "Ovarian Dysmetabolic Syndrome" offers a more comprehensive and accurate representation of the condition traditionally known as PCOS. This nomenclature highlights both the ovarian and metabolic dysfunctions that define the syndrome, encompassing a broader spectrum of phenotypes beyond hyperandrogenism. Compared to other suggested terms, "Ovarian Dysmetabolic Syndrome" provides the necessary balance between specificity and inclusivity, addressing the reproductive and metabolic aspects without being overly restrictive. By adopting this terminology, we can better align the syndrome with its diverse clinical presentations and underlying pathophysiology, ultimately improving both diagnosis and management strategies. These proposed names acknowledge the broad impact of PCOS on multiple organ systems and address the need for a more accurate depiction of the syndrome's pathophysiology.

The potential impact of renaming PCOS is substantial. A more descriptive name could enhance diagnostic accuracy, improve patient education, and support a more holistic approach to management that addresses both metabolic and reproductive health. It would also help reduce stigma and confusion associated with the term "polycystic," which may not fully capture the syndrome's multi-systemic nature. Healthcare providers must continue to educate patients about the comprehensive nature of PCOS, including its metabolic and hormonal aspects. Regardless of the terminology used, the focus should remain on delivering comprehensive care that addresses all facets of the condition to improve patient outcomes and overall health.

Declarations

Ethics Approval and Consent to Participate

No patients were involved in this review. This study has been approved by the ethics committee of the faculty of medicine of Sousse.

Consent for Publication

Not applicable.

Authors Contributions

Dr. Ach Taieb drafted the manuscript, while Dr. Methnani Jabeur read and approved the final version. Gorchane Asma contributed to the manuscript drafting. Ben Abdessalem Fatma, Ben Haj Slama Nassim, and Ben Abdelkrim Asma provided critical revisions in their respective areas.

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Availability of Data and Materials

The collected data is available upon request from the authors of the study.

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REFERENCES

1. Sadeghi HM, Adeli I, Calina D, et al. Polycystic ovary syndrome: a comprehensive review of pathogenesis, management, and drug repurposing. *Int J Mol Sci*. 2022;23(2):583.
2. Deswal R, Narwal V, Dang A, Pundir CS. The prevalence of polycystic ovary syndrome: a brief systematic review. *J Hum Reprod Sci*. 2020;13:261-271.
3. Hoyt KL, Schmidt MC. Polycystic ovary (stein-Leventhal) syndrome: etiology, complications, and treatment. *Clin Lab Sci*. 2004;17:155-163.
4. Lentscher JA, Decherney AH. Clinical presentation and diagnosis of polycystic ovarian syndrome. *Clin Obstet Gynecol*. 2021;64:3-11.
5. Sanchez-Garrido MA, Tena-Sempere M. Metabolic dysfunction in polycystic ovary syndrome: pathogenic role of androgen excess and potential therapeutic strategies. *Mol Metab*. 2020;35:100937.
6. Harada M. Pathophysiology of polycystic ovary syndrome revisited: Current understanding and perspectives regarding future research. *Reprod Med Biol*. 2022;21:e12487.
7. Singh S, Pal N, Shubham S, et al. Polycystic ovary syndrome: etiology, current management, and future therapeutics. *J Clin Med*. 2023;12(4):1454.
8. Piltonen TT, Ruokojärvi M, Karro H, et al. Awareness of polycystic ovary syndrome among obstetrician-gynecologists and endocrinologists in Northern Europe. *PLoS One*. 2019;14:e0226074.
9. Martin ML, Halling K, Eek D, Krohe M, Paty J. Understanding polycystic ovary syndrome from the patient perspective: a concept elicitation patient interview study. *Health Qual Life Outcomes*. 2017;15:162.
10. Khadilkar SS. Polycystic ovarian syndrome: is it time to rename PCOS to ha-pods? *J Obstet Gynaecol India*. 2016;66:81-87.
11. Azziz R. Polycystic ovary syndrome: what's in a name? *J Clin Endocrinol Metab*. 2014;99:1142-1145.
12. Ach T, Guesmi A, Kalboussi M, et al. Validation of the follicular and ovarian thresholds by an 18-MHz ultrasound imaging in polycystic ovary syndrome: a pilot cutoff for North African patients. *Ther Adv Reprod Health*. 2024;18:26334941241270372.
13. Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. *Am J Obstet Gynecol*. 1935;29:181-191.
14. Szydlarska D, Machaj M, Jakimiuk A.History of discovery of polycystic ovary syndrome. *Adv Clin Exp Med*. 2017;26:555-558.
15. Azziz R. A brief history of androgen excess. In: Azziz R, Nestler J, Dewailly D eds. *Androgen Excess Disorders in Women: Polycystic Ovary Syndrome and Other Disorders*. Humana Press; 2007:3-16.
16. McArthur JW, Ingersoll FM, Worcester J. The urinary excretion of interstitial-cell and follicle-stimulating hormone activity by women with diseases of the reproductive system. *J Clin Endocrinol Metab*. 1958;18:1202-1215.
17. Yen SS, Vela P, Rankin J. Inappropriate secretion of follicle-stimulating hormone and luteinizing hormone in polycystic ovarian disease. *J Clin Endocrinol Metab*. 1970;30:435-442.
18. Swanson M, Sauerbrei EE, Cooperberg PL. Medical implications of ultrasonically detected polycystic ovaries. *J Clin Ultrasound*. 1981;9:219-222.
19. Shoupe D, Kumar DD, Lobo RA. Insulin resistance in polycystic ovary syndrome. *Am J Obstet Gynecol*. 1983;147:588-592.
20. Franks S, Adams J, Mason H, Polson D. Ovulatory disorders in women with polycystic ovary syndrome. *Clin Obstet Gynaecol*. 1985;12:605-632.
21. Zawadzki J, Dunaif A, Givens J, Haseltine F, Merriam G. *Polycystic Ovary Syndrome, Current Issues in Endocrinology and Metabolism*. Blackwell Scientific Publications; 1992.
22. Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19:41-47.
23. Azziz R, Carmina E, Dewailly D, et al. Positions statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an androgen excess society guideline. *J Clin Endocrinol Metab*. 2006;91:4237-4245.
24. Teede HJ, Misso ML, Costello MF, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod*. 2018;33:1602-1618.
25. Teede HJ, Tay CT, Laven JJE, et al. Recommendations from the 2023 International Evidence-based guideline for the assessment and management of polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2023;108:2447-2469.
26. Witchel SF, Oberfield SE, Peña AS. Polycystic ovary syndrome: pathophysiology, presentation, and treatment with emphasis on adolescent girls. *J Endocr Soc*. 2019;3:1545-1573.
27. Franks S, Gharani N, McCarthy M. Candidate genes in polycystic ovary syndrome. *Hum Reprod Update*. 2001;7:405-410.
28. Khan MJ, Ullah A, Basit S. Genetic basis of polycystic ovary syndrome (PCOS): current perspectives. *Appl Clin Genet*. 2019;12:249-260.
29. Joo YY, Actkins K, Pacheco JA, et al. A polygenic and phenotypic risk prediction for polycystic ovary syndrome evaluated by phenome-wide association studies. *J Clin Endocrinol Metab*. 2020;105:1918-1936.
30. Hiam D, Moreno-Asso A, Teede HJ, et al. The genetics of polycystic ovary syndrome: an overview of candidate gene systematic reviews and genome-wide association studies. *J Clin Med*. 2019;8(10):1606.
31. Bogari NM. Genetic construction between polycystic ovarian syndrome and type 2 diabetes. *Saudi J Biol Sci*. 2020;27:2539-2543.
32. Welt CK. Genetics of polycystic ovary syndrome: what is new? *Endocrinol Metab Clin North Am*. 2021;50:71-82.
33. Dumesic DA, Goodarzi MO, Chazenbalk GD, Abbott DH. Intrauterine environment and polycystic ovary syndrome. *Semin Reprod Med*. 2014;32:159-165.
34. Hart R. Generational health impact of PCOS on women and their children. *Med Sci*. 2019;7(3):49.
35. Ye W, Xie T, Song Y, Zhou L. The role of androgen and its related signals in PCOS. *J Cell Mol Med*. 2021;25:1825-1837.
36. Zhu W, Han B, Fan M, et al. Oxidative stress increases the 17,20-lyase-catalyzing activity of adrenal P450c17 through p38α in the development of hyperandrogenism. *Mol Cell Endocrinol*. 2019;484:25-33.
37. Franks S, Hardy K. Androgen action in the ovary. *Front Endocrinol*. 2018;9:452.
38. Rezgoun ML, El Khour D, Bendaoud H, Chellat D. CYP17A1 (rs74357) polymorphism and polycystic ovary syndrome risk: a systemic review and meta-analysis. *Acta Biomed*. 2023;94:e2023167.
39. Xu Y, Qiao J. Association of insulin resistance and elevated androgen levels with polycystic ovarian syndrome (PCOS): a review of literature. *J Healthc Eng*. 2022;2022:9240569.
40. Reddy BM, Kommoju UJ, Dasgupta S, Rayabarapu P. Association of type 2 diabetes mellitus genes in polycystic ovary syndrome aetiology among women from southern India. *Indian J Med Res*. 2016;144:400-408.
41. Rosenfield RL. Current concepts of polycystic ovary syndrome pathogenesis. *Curr Opin Pediatr*. 2020;32:698-706.
42. Malini NA, Roy GK. Influence of insulin on LH, testosterone and SHBG in various PCOS categories based on the mode of secretion of LH in relation to FSH Levels. *Acta Endocrinol*. 2021;17:313-318.
43. di Clemente N, Racine C, Rey RA. Anti-müllerian hormone and polycystic ovary syndrome in women and its male equivalent. *Biomedicines*. 2022;10(10):2506.
44. Ran Y, Yi Q, Li C. The relationship of anti-mullerian hormone in polycystic ovary syndrome patients with different subgroups. *Diabetes Metab Syndr Obes*. 2021;14:1419-1424.
45. McCartney CR, Campbell RE, Marshall JC, Moenter SM. The role of gonadotropin-releasing hormone neurons in polycystic ovary syndrome. *J Neuroendocrinol*. 2022;34:e13093.
46. Witchel SF, Tena-Sempere M. The kiss1 system and polycystic ovary syndrome: lessons from physiology and putative pathophysiologic implications. *Fertil Steril*. 2013;100:12-22.
47. Moore AM, Lohr DB, Coolen LM, Lehman MN. Prenatal androgen exposure alters KNDy neurons and their afferent network in a model of polycystic ovarian syndrome. *Endocrinology*. 2021;162(11):bqab158.
48. Lobo RA. A disorder without identity: "HCA," "pco," "pcod," "pcos," "sls." what are we to call it?! *Fertil Steril*. 1995;63:1158-1160.

49. Behera M, Price T, Walmer D. Estrogenic ovulatory dysfunction or functional female hyperandrogenism: an argument to discard the term polycystic ovary syndrome. *Fertil Steril*. 2006;86:1292-1295.
50. Teede H, Gibson-Helm M, Norman RJ, Boyle J. Polycystic ovary syndrome: perceptions and attitudes of women and primary health care physicians on features of PCOS and renaming the syndrome. *J Clin Endocrinol Metab*. 2014;99: E107-E111.
51. Arima H, Cheetham T, Christ-Crain M, et al. Changing the name of diabetes insipidus: a position statement of the working group for renaming diabetes insipidus. *J Clin Endocrinol Metab*. 2022;108:1-3.
52. Hughes IA, Houk C, Ahmed SF, Lee PA. Consensus statement on management of intersex disorders. *Arch Dis Child*. 2006;91:554-563.
53. Bahadori F, Jahanian Sadatmahalleh S, Montazeri A, Nasiri M. Sexuality and psychological well-being in different polycystic ovary syndrome phenotypes compared with healthy controls: a cross-sectional study. *BMC Womens Health*. 2022;22:390.
54. Ranasinghe BA, Balasuriya A, Wijeyaratne CN, Fernando N. The impact of peer-led support groups on health-related quality of life, coping skills and depressive symptomatology for women with PCOS. *Psychol Health Med*. 2023; 28:564-573.
55. Barber TM, Dimitriadis GK, Andreou A, Franks S. Polycystic ovary syndrome: insight into pathogenesis and a common association with insulin resistance. *Clin Med*. 2016;16:262-266.
56. Lau GM, Elghobashy M, Thanki M, et al. A systematic review of lived experiences of people with polycystic ovary syndrome highlights the need for holistic care and co-creation of educational resources. *Front Endocrinol*. 2022;13: 1064937.
57. Bazarganipour F, Ziaei S, Montazeri A, et al. Psychological investigation in patients with polycystic ovary syndrome. *Health Qual Life Outcomes*. 2013; 11:141.
58. Young CC, Rew L, Monge M. Transition to self-management among adolescents with polycystic ovary syndrome: parent and adolescent perspectives. *J Pediatr Nurs*. 2019;47:85-91.
59. Schoch CL, Ciufo S, Domrachev M, et al. NCBI Taxonomy: a comprehensive update on curation, resources and tools. *Database*. 2020;2020:baaa062.
60. Elhariry M, Malhotra K, Solomon M, Goyal K, Kempegowda P. Top 100 #PCOS influencers: understanding who, why and how online content for PCOS is influenced. *Front Endocrinol*. 2022;13:1084047.
61. Akre S, Sharma K, Chakole S, Wanjari MB. Recent advances in the management of polycystic ovary syndrome: a review article. *Cureus*. 2022;14:e27689.
62. Azziz R. Polycystic ovary syndrome. *Obstet Gynecol*. 2018;132:321-336.
63. Traub ML. Assessing and treating insulin resistance in women with polycystic ovarian syndrome. *World J Diabetes*. 2011;2:33-40.
64. Teede H, Deeks A, Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. *BMC Med*. 2010;8:41.
65. Barber TM, Hanson P, Weickert MO, Franks S. Obesity and polycystic ovary syndrome: Implications for pathogenesis and novel management strategies. *Clin Med Insights Reprod Health*. 2019;13:1179558119874042.
66. Sam S. Obesity and polycystic ovary syndrome. *Obes Manag*. 2007;3:69-73.
67. Cunha A, Póvoa AM. Infertility management in women with polycystic ovary syndrome: a review. *Porto Biomed J*. 2021;6:e116.
68. Kayali S, Chitra T, Kamalanathan S, Nandeesha H. Assessment of metabolic syndrome in infertile women with polycystic ovary syndrome in a rural population of South India: a cross-sectional study. *Int J Reprod Biomed*. 2022;20:161-168.
69. Moran LJ, Misso ML, Wild RA, Norman RJ. Impaired glucose tolerance, type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: a systematic review and meta-analysis. *Hum Reprod Update*. 2010;16:347-363.
70. Ligocka N, Chmaj-Wierzchowska K, Wszołek K, Wilczak M, Tomczyk K. Quality of life of women with polycystic ovary syndrome. *Medicina*r. 2024;60:294.
71. Scicchitano P, Dentamaro I, Carbonara R, et al. Cardiovascular risk in women with PCOS. *Int J Endocrinol Metab*. 2012;10:611-618.
72. Amiri M, Ramezani Tehrani F, Behboudi-Gandevani S, Bidhendi-Yarandi R, Carmina E. Risk of hypertension in women with polycystic ovary syndrome: a systematic review, meta-analysis and meta-regression. *Reprod Biol Endocrinol*. 2020;18:23.
73. Kargili A, Karakurt F, Kasapoglu B, et al. Association of polycystic ovary syndrome and a non-dipping blood pressure pattern in young women. *Clinics*. 2010; 65:475-479.
74. Dason ES, Koshkina O, Chan C, Sobel M. Diagnosis and management of polycystic ovarian syndrome. *CMAJ*. 2024;196:E85-E94.
75. Taieb A, Majdoub M, Souissi N, Chelly S, Ben Abdelkrim A. Determination of the contributing factors and HbA1c cutoff leading to glucose tolerance abnormalities following gestational diabetes. *Cureus*. 2024;16:e56218.
76. Forslund M, Melin J, Stener-Victorin E, et al. International evidence-based guideline on assessment and management of PCOS-a nordic perspective. *Acta Obstet Gynecol Scand*. 2024;103:7-12.
77. Cowan S, Lim S, Alycia C, et al. Lifestyle management in polycystic ovary syndrome - beyond diet and physical activity. *BMC Endocr Disord*. 2023;23:14.
78. Methnani J, Hajbelgacem M, Ach T, et al. Effect of pre-meal metformin with or without an acute exercise bout on postprandial lipemic and glycemic responses in metabolic syndrome patients: a randomized, open label, crossover study. *J Cardiovasc Pharmacol Ther*. 2023;28:10742484231156318.
79. Ravn P, Gram F, Andersen MS, Glintborg D. Myoinositol vs. metformin in women with polycystic ovary syndrome: a randomized controlled clinical trial. *Metabolites*. 2022;12(12):1183.