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POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Polycystic Ovarian Syndrome (PCOS) is a multifaceted endocrine condition impacting women of reproductive age, marked by symptoms including hyperandrogenism, irregular menstrual cycles, and the presence of polycystic ovaries. Although it is common and significantly affects women's health, the pathogenesis of PCOS is still not fully understood. This review offers an extensive critical evaluation of the current literature regarding PCOS pathogenesis, identifying areas lacking knowledge and emphasizing its multifactorial character. A thorough literature review found pertinent articles published up to the knowledge cutoff in 2023, emphasizing molecular, genetic, hormonal, and environmental elements that play a role in the development of PCOS. Electronic databases such as PubMed, MEDLINE, and Embase were thoroughly searched utilizing specific terms. Qualified studies explored molecular, genetic, hormonal, and environmental elements linked to the development of PCOS. The critical evaluation uncovered various studies that enhance our comprehension of PCOS. Molecular and genetic research has emphasized changes in signaling pathways, hormonal imbalances, and the impact of insulin resistance. Environmental factors, such as lifestyle choices and exposure to endocrine-disrupting substances, were involved. Variability in research designs and methods emphasized the necessity for standardized approaches to improve comparability. This review consolidates existing evidence on the critical assessment and development of PCOS, highlighting its complex nature. Standardizing study designs and methods will enable future comparisons, fostering the creation of targeted therapeutic approaches and personalized management plans for women impacted by PCOS.

KEYWORDS: Polycystic ovary syndrome; Knowledge; Attitude; Complications.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common condition, with estimates suggesting it impacts 5-10% of women in their reproductive years1. This makes it the most prevalent endocrine condition in this group.[1] Polycystic ovary syndrome (PCOS) consists of a collection of symptoms resulting from increased androgens (male hormones) in women. Indicators and manifestations of PCOS consist of irregular or absent menstrual cycles, heavy bleeding, excessive body and facial hair, acne, pelvic discomfort, challenges in achieving pregnancy, and areas of thick, darker, and velvety skin. Related conditions encompass type 2 diabetes, obesity, obstructive sleep apnea, heart disease, mood disorders, and endometrial cancer.[2] In a publication by Ibanez et al., new diagnostic guidelines for PCOS were suggested, tailored to younger patients where irregular menstrual cycles and clinical and/or biochemical hyperandrogenism were identified as diagnostic criteria. According to the criteria for diagnosing PCOS in adolescents suggested by Pena et al.[3]

Together, these impacts will influence their quality of life. Raising awareness through effective counseling can lead to meaningful changes in the attitudes and behaviors of women with PCOS. Students of health science will take on an important role in this area as they learn about the prevention and treatment of different illnesses. There have been no prior studies that assessed the quality of life of pharmacy students with PCOS and offered guidance on the condition. Therefore, we sought to evaluate the quality of life of pharmacy students diagnosed with PCOS. The Quality of Life questionnaire for Polycystic Ovarian Syndrome (PCOSQ).[4]

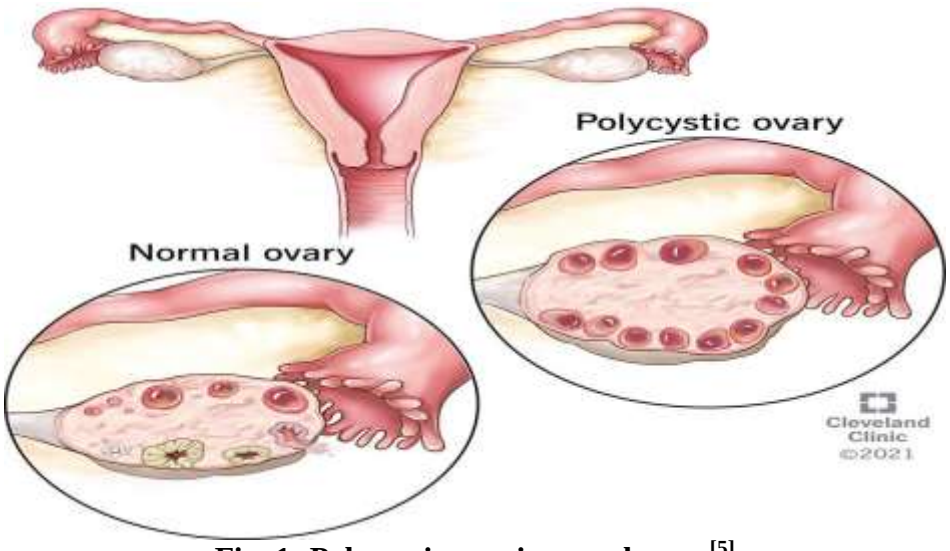

Fig. 1: Polycystic ovarian syndrome.[5]

PCOS is evidently a frequent reason for hirsutism and anovulation, and it is linked to intrinsic insulin resistance in numerous women. This condition impacts nearly 6% of women of reproductive age and often arises soon after the onset of menstruation. Despite significant differences in opinions regarding diagnostic criteria, the majority of healthcare professionals adhere to the guidelines established by the 1990 National Institutes of Health (NIH) Consensus Conference.[6] PCOS is among the most prevalent endocrine-reproductive metabolic disorders in people, impacting 5–15% of women globally, based on the standards applied. The signs of PCOS consist of somewhat differing hyperandrogenism (HA), ovulatory dysfunction (OD), polycystic ovarian morphology (PCOM), gonadotropic irregularities, along with insulin resistance (IR) and compensatory hyperinsulinism. The condition is regarded as a multifaceted genetic characteristic with significant heritable factors. While various criteria exist to define the disorder, what matters more is the necessity to precisely characterize the phenotype of the patient in question. PCOS phenotypes can typically be divided, in their most basic forms, into four categories: (a) Phenotype A, showing signs of HA, whether clinical, like hirsutism, and/or biochemical, such as hyperandrogenemia, along with OD, often indicated by menstrual irregularities, and PCOM; (b) phenotype B, which has HA and OD, but excludes PCOM; (c) phenotype C, comprising HA and PCOM, yet lacking OD; and (d) phenotype D, featuring OD and PCOM, but not HA. From a metabolic standpoint, phenotypes A and B (referred to as “classic PCOS”) exhibit comparable behaviors, with around 75–85% showing insulin resistance and some type of metabolic dysfunction. These people face a higher risk of glucose intolerance and diabetes. Conversely, women with phenotype D of PCOS (known as “nonhyperandrogenic PCOS”), who do not show clear signs of high androgen levels, have minimal indication of metabolic dysfunction and face a low risk of experiencing glucose intolerance disorders. Individuals with phenotype C (commonly called "ovulatory PCOS") exhibit levels of metabolic dysfunction and risk that are somewhat lower than those with the classic types of PCOS, yet still significantly higher than those of control subjects or women with nonhyperandrogenic PCOS. Reproductively, women with OD will clearly show higher levels of subfertility compared to ovulatory PCOS patients.[7]

Pathophysiology

Polycystic ovary syndrome is a condition that impacts numerous women of reproductive age. The occurrence of PCOS differs based on the population's age group, ethnicity, and the

diagnostic criteria used. An increasing number of studies indicate that this issue does not solely impact young women, but it can start during adolescence.

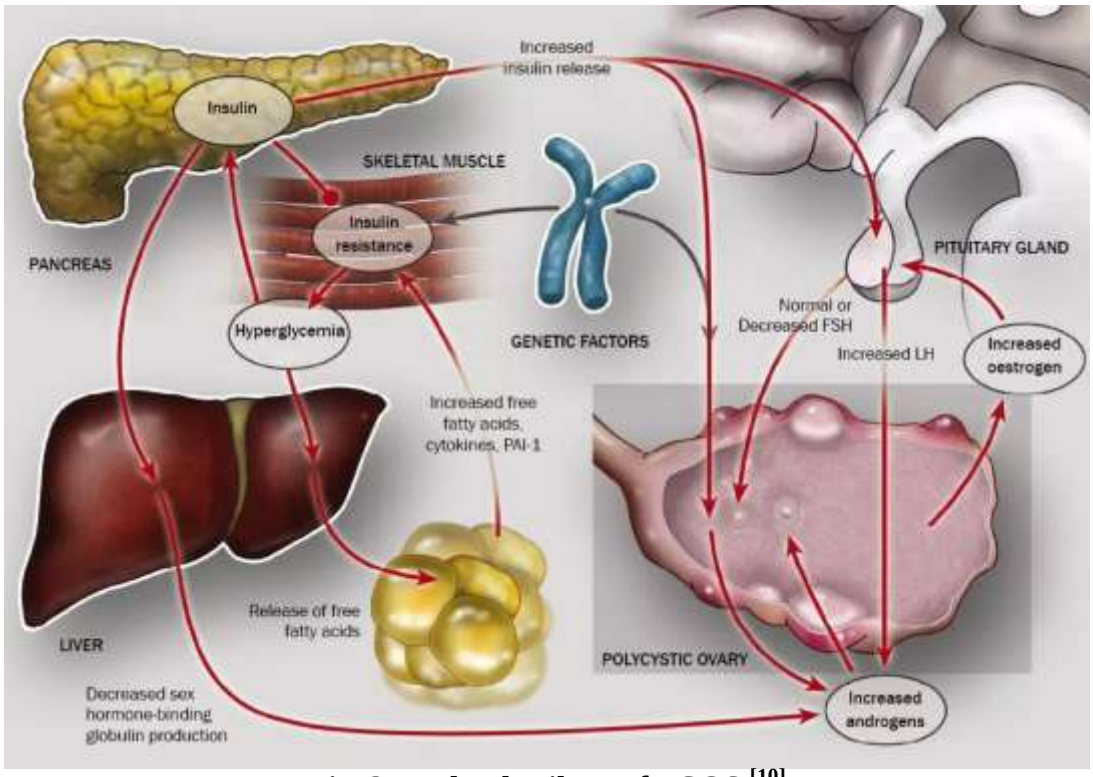

Fig. 2: Pathophysilogy of PCOS.[10]

A study on a population of Korean women revealed that the age-adjusted prevalence of PCOS was 2.8%, with an increase during late adolescence, reaching its highest point at age 20 and starting to decrease by age 30.[8] In research conducted on girls from South India, the occurrence of PCOS was found to be 6.8%. The majority of study participants identified with PCOS were unaware of their condition (78.4%), whereas 6.8% had previously received treatment for PCOS. The primary sources of information on PCOS were predominantly teachers (37%), followed by doctors (31.5%), the Internet (11%), and friends (7.5%). Awareness of polycystic ovary syndrome was greater in young women (84.9%) than in adolescent girls (4.5%). The most significant factor contributing to the low awareness level was deemed to be insufficient information and publicity (63%), highlighting the necessity for effective health education and the establishment of initiatives to elevate awareness and address PCOS issues among adolescents.[9]

Causes

- Polycystic ovary syndrome
- Cushing's syndrome- high levels of the hormone cortisol

- Congenital adrenal hyperplasia- This inherited condition is characterized by abnormal production of steroid hormones, including cortisol and androgen, by adrenal glands.
- Tumors- Rarely, an androgen-secreting tumor in the ovaries or adrenal glands may cause hirsutism
- Medications- Some medications can cause hirsutism. One such drug is danazol, which is used to treat women with endometriosis.[11]
- Not clearly known yet.
- May be change in lifestyle, diet and stress.
- Genetic factors: CYP21 gene mutation
- Runs in families!!
- Obesity causing Insulin resistance & hyperinsulinemia.[10]

Long-term consequences

- **Endometrial and Ovarian cancer:** In PCOS, estrogen's effect on the endometrium is unopposed due to lack of cyclical progesterone, thus predisposing to endometrial cancer. In the ovary, the inability to produce estradiol because of the decreased activity of FSH-related aromatase attenuates the development of ovulatory follicles, thereby causing the development of a large number of follicles in various stages of arrested maturation and accelerated senescence, giving rise to the typical picture of polycystic ovaries, while also producing higher levels of inhibin, accentuating the FSH suppression. Furthermore, the lack of follicular maturation causes anovulation, while the low or normal estradiol levels together with the elevated estrone predispose to the unopposed growth of the endometrium. The lack of cyclical progesterone because of anovulation allows for unopposed endometrial growth, which is only partially shed during episodes of dysfunctional uterine bleeding, predisposing to the later development of endometrial cancer. At the same time, the tonic and abnormal stimulation of the ovary is thought to be related to a higher incidence of ovarian cancer in later years in these patients.[12]

- **Coronary artery disease:** Insulin resistance is the underlying pathological cause of the recently identified metabolic syndrome, which is characterized by an increased waist circumference (> 35 inches in women), low levels of high-density lipoprotein cholesterol (HDL), elevated triglycerides, high blood pressure (> 130/80 mm Hg), and elevated fasting glucose (> 100 mg/dL). This article does not aim to explain how insulin resistance specifically leads to various factors, but it is important to note that the occurrence of

coronary artery disease is two to five times greater in those with the syndrome, which is prevalent in the later stages of many patients with PCOS.[13]

- PCOS is associated with an increased risk of type 2 diabetes and cardiovascular events.
- Possible risk of sleep apnoea.
- Oligo- or amenorrhoea in women with PCOS may predispose to endometrial hyperplasia and later carcinoma. It is good practice to recommend treatment with Progestogens to induce a withdrawal bleed at least every 3 to 4 months.[11]

Diagnosis

The identification of PCOS is mainly based on clinical evaluation. In 1990, a consensus conference organized by the National Institutes of Health (NIH) recommended that the diagnostic criteria should include characteristics of hyperandrogenism along with chronic anovulation, once identifiable causes are ruled out. Menarche can be either normal or delayed, and it may be accompanied by amenorrhea, oligomenorrhea, or dysfunctional uterine bleeding.[14] The diagnosis of PCOS in teenage girls remains a debated and extensively studied issue. There are numerous uncertainties regarding which characteristics can still be regarded as physiological for the maturation process and which exceed the standard. The diagnostic criteria for adults do not align with the diagnosis for this particular group of adolescent patients. There are still active research efforts examining the distinctions in diagnosing adults versus adolescents, the cut-off thresholds for diagnostic criteria, and new factors that could aid in diagnosis. To explore the variations in PCOS between adult and adolescent patients, a study was carried out that assessed clinical, hormonal, biochemical, and ultrasound parameters. Curiously, this research uncovered no statistically meaningful difference in PCOS among adults and teenagers. The menstrual cycles of adolescent and adult PCOS patients showed no significant differences. In laboratory research, the average serum ratios of LH/FSH (luteinizing hormone/follicle-stimulating hormone), free testosterone, and insulin were notably elevated in both adults and adolescents with PCOS when compared to the control group.[15]

Anti-Mullerian hormone (AMH) is a well-researched factor. Research indicates that AMH levels were notably elevated in adolescents diagnosed with PCOS compared to controls. According to the meta-analysis, AMH cut-off levels for diagnosing PCOS in adolescents were determined — varying by study, they were 6.1, 6.26, 7.03, 7.11, 7.2, and 7.25 ng/mL (diagnostic accuracy being 81% for specificity and 66.3% for sensitivity). This research

indicated that the AMH level test with an estimated threshold of 6–7 ng/mL can serve as a diagnostic tool for PCOS in teenagers.[16]

Symptoms

- **Menstrual disturbance**

In the biggest study of women with PCOS, it is noted that among the 1871 women exhibiting at least one symptom of PCOS (according to older diagnostic guidelines), roughly 30% experienced a regular menstrual cycle, 50% had oligomenorrhea, and 20% suffered from amenorrhea. As a result, most women with PCOS experience irregular menstrual cycles, with the most common pattern being infrequent periods linked to ovulation.

Goldzieher and Green proposed that around 85–90% of women experiencing oligomenorrhea, and as many as 30–40% of those with amenorrhea, are likely to have PCOS. Obesity seems to enhance anovulation in PCOS by raising peripheral estrogen production and increasing pancreatic insulin output, which disrupts the hypothalamic–pituitary–ovarian (HPO) axis, leading to higher LH levels that hinder follicular maturation. Gaining weight could lead to oligo- or amenorrhea, while losing weight can bring back ovulation and regular menstrual cycles.

- **Obesity**

The documented frequency of obesity in women suffering from PCOS largely relies on the kind of clinic the patient visits and the diagnostic standards applied. Nonetheless, in many extensive studies, 35–50% of women with PCOS are either overweight (BMI >25) or obese (BMI >27 kg/m^2). Abdominal fat accumulation is prevalent, characterized by an elevated waist-hip ratio. Obesity raises the likelihood of type-2 diabetes, and as many as 30% of obese women with PCOS experience IGT, while an additional 7.5% will progress to full-blown diabetes by their forties. Central obesity is believed to be a major contributor to the seven-fold heightened risk of myocardial infarction in women affected by PCOS. Nonetheless, the positive impacts of weight reduction are consistently demonstrated in enhancing menstrual cycle regularity, reinstating ovulation, and normalizing biochemical markers, especially insulin resistance. Given the widespread occurrence of IGT and type-2 diabetes in obese women facing PCOS, the consensus group recommends that obese women (BMI >27 kg/m2) with PCOS undergo screening using an oral glucose tolerance test.

- **Acne**

Acne is an inflammatory condition affecting the hair follicle along with its related sebaceous and apocrine glands. It is found in as many as one-third of women affected by PCOS. In contrast to androgenic alopecia and hirsutism, the main issue for women suffering from acne is excessive sebaceous output, and blood androgen levels are frequently not elevated.

- **Acanthosis nigricans**

Acanthosis nigricans is a skin condition that primarily appears in areas such as the armpits, skin folds, and at the back of the neck. It is evident through heightened pigmentation and papillomatosis. It is a marker linked to IR and a compensatory rise in insulin secretion. It is estimated to occur in women with PCOS in approximately 1 to 3% of instances 14, 44 and may appear more frequently in adolescents diagnosed with PCOS.[17]

Treatment

In the 1930s, Stein and Cohen28 discovered by chance that ovarian wedge resection resulted in the return of regular menstrual cycles and sometimes pregnancy. Regrettably, the syndrome resurfaced in the majority of patients. The conventional management of PCOS focuses on the clinical symptoms and relies on the aspects that trouble the patient the most. The response to treatment is gradual, with biochemical improvement occurring 6 to 9 months before any clinical changes are observed. Addressing acne, hirsutism, and menstrual irregularities when fertility is not a concern necessitates a collaborative approach on multiple levels.[18]

- **Nonpharmacologic measures**

Nonpharmacologic strategies are universally advised; they encompass diet, exercise, and weight loss if obese or to restore a level of insulin sensitivity. While long-term success may vary and maintaining adherence can be difficult, research indicates a notable decrease in androgens and a return to ovulatory cycles with a weight loss of just 10 to 15 pounds over six months.29 Improvements in hirsutism can be observed within the first 6 to 9 months, alongside weight loss, and regular menstrual cycles may occur simultaneously with reduced androgen levels. The metabolic effects of PCOS can also enhance through non-drug interventions, leading to decreases in hyperinsulinemia, ovarian P450c17 activity, plasminogen activator inhibitor-1 activity, and triglycerides, alongside a simultaneous rise in HDL cholesterol.[19]

There is scant evidence directly linking multidisciplinary PCOS clinics to the effectiveness of their treatment. It is widely recognized that PCOS is complex and exhibits significant variability among those affected by the syndrome. When managing a patient with PCOS, it is essential to address the patient's immediate needs while minimizing the chances of long-term risk factors. Symptoms will be more effectively managed when the patient receives care from multiple specialists collaborating together. When people encounter various providers, it is less probable that a PCOS diagnosis will be overlooked. The earlier PCOS is detected and therapy starts, the better the prognosis and quality of life for the condition will be. The recognized advantages of multidisciplinary clinics worldwide encompass enhanced patient satisfaction, increased weight loss, improved body image, and more effective holistic management of PCOS. More investigations are required to evaluate other current multidisciplinary clinics to gauge patient satisfaction and treatment outcomes in comparison to individuals receiving care from a sole provider. Further research is necessary to enhance understanding of evidence-based guidelines for managing PCOS, particularly regarding dietary advice.[20]

The summarized literature clearly shows that a wide range of pharmacotherapies with different potential advantages exists for managing PCOS. It is crucial to recognize that no one agent can tackle the whole range of issues (Endocrine, Metabolic and Clinical) that may arise in a woman with a PCOS diagnosis due to the varied characteristics of the syndrome. Hormonal approaches like COCs can effectively manage menstrual irregularities, provide skin advantages against hyperandrogenic symptoms, and protect the endometrium from proliferative pathologies, but will not alleviate the metabolic issues associated with PCOS. Likewise, antiandrogen treatment mainly focuses on the skin manifestations of HA and may enhance menstrual regularity as a secondary benefit; considering a potential boost in ovulatory response from antiandrogen therapy along with its known teratogenic risks, the importance of utilizing a dependable contraceptive method should be emphasized when providing antiandrogen therapy to women with PCOS. The safety and effectiveness of metformin in providing metabolic advantages in PCOS are well documented. While not as effective as CC for inducing ovulation, metformin, when used alongside ovulation-inducing methods, may enhance reproductive results, especially in obese women with PCOS, and can improve treatment response in those considered resistant to CC. TZDs provide minimal advantages compared to metformin for treating PCOS-related insulin resistance and should be avoided by women planning for pregnancy. Although the metabolic advantages and

enhancements in PCOS-related hyperandrogenemia are greater with statins compared to metformin alone, statins, like TZDs, should be avoided in women who are trying to conceive. Incretins represent a promising group of metabolic regulators and deserve additional research in the PCOS demographic. Utilizing MYO is a straightforward and secure approach that has demonstrated effectiveness for biochemical and clinical outcomes in managing PCOS and deserves more attention.[21]

In summary, PCOS is increasingly common among women of reproductive age, leading to lifelong complications. One of the toughest features of this syndrome is its unclear diagnostic standards and the extensive intricacy of traits. Future studies on the genetics and pathophysiology of PCOS are essential to identify preventive risk factors and effective treatment strategies for this syndrome.[22] Women with PCOS possess multiple risk factors for the development of type-2 diabetes, such as central obesity, issues with insulin action and secretion, and a family history of type-2 diabetes. They also possess elevated levels of cardiovascular risk factors: insulin resistance, obesity, dyslipidemia, and hypertension. Irregular menstrual cycles could be an extra risk factor.[23]

- **Acarbose**

The therapeutic effectiveness of acarbose is due to its ability to lower glucose absorption in the intestine, which in turn reduces post-meal insulin levels. The possible function of acarbose in PCOS has been investigated, yet its impact on insulin sensitivity measures, body weight, and vascular health varied, with no noteworthy enhancement in PCOS-related dyslipidemia. Negative effects, mainly related to the gastrointestinal system, are frequent, and there have been reports of potentially lethal hepatotoxicity. Variable effectiveness, troublesome side effects, and the potential for liver harm restrict the use of this agent in clinical settings.

- **Stereoisomers of inositol**

Inositol belongs to the Vitamin B complex group; two of its stereoisomers, D-chiro-inositol (DCI) and myo-inositol (MYO), have been investigated to assess their potential to enhance insulin sensitivity and their significance in managing PCOS. While earlier studies indicated that DCI might be effective, later findings did not support its efficacy in PCOS. MYO, on the other hand, has demonstrated reliable potential.

- **Cholesterol-reducing medications (Statins)**

In women with PCOS, it is common to observe raised serum LDL and triglycerides alongside lowered high-density lipoprotein levels. 1–3, Statins reduce cholesterol production, lowering circulating LDL cholesterol levels, and provide a rational therapeutic advantage for dyslipidemic women identified as being at an increased risk of cardiovascular disease. The use of statins is linked to a 20% reduction in cardiovascular mortality for every mmol/l of LDL cholesterol decrease attained.[24]

CONCLUSION

Polycystic ovary syndrome is a condition impacting an increasing number of teenage girls and young women globally, greatly influencing their mental health, reproductive health, and overall quality of life. It is linked to numerous complications that greatly impact the overall health of the patient and necessitate the participation of a multidisciplinary team. Given the multimorbidity associated with patients who have PCOS, early diagnosis is essential, ideally during the teenage years, to initiate treatment and interrupt the metabolic progression of PCOS effects, thus preventing later complications in adult life. The cause of PCOS is still unclear, yet it is definitely intricate and involves multiple factors. The impact of genetic, environmental, and lifestyle elements is examined to grasp the nature of this illness. We are increasingly aware of the factors contributing to the onset of PCOS, which could begin well before birth. Additional studies are required to determine the factors and reasons that contribute to the onset of polycystic ovary syndrome. Debates continue about the diagnosis of PCOS in teenage girls and which criteria are suitable for this age group. Research investigating the threshold values of diagnostic parameters can offer us considerable new insights into diagnostic processes and elucidate the established diagnostic boundaries. Thorough characterization of extensive cohorts of adolescent PCOS patients and meticulous examination of data would aid in resolving numerous inquiries regarding the prevalence of this condition disorder in teenagers. The prevalence of PCOS in adolescent girls clearly poses a challenge for both physicians providing patient care and for researchers encountering numerous uncertainties to explore.

REFERANCE

1. McGowan MP. Polycystic ovary syndrome: a common endocrine disorder and risk factor for vascular disease. Current treatment options in cardiovascular medicine, 2011; 13(4): 289-301.

2. Available from: https://www.en.wikipedia.org/wiki/Polycystic_ovary_syndrome. [Last accessed on 2018 Dec 27
3. Peña AS, Codner E, Witchel S. Criteria for Diagnosis of Polycystic Ovary Syndrome during Adolescence: Literature Review. Diagnostics (Basel), 2022; 12(8), doi: 10.3390/diagnostics12081931, indexed in Pubmed: 36010282
4. Cronin L, Guyatt G, Griffith L, Wong E, Azziz R, Futterweit W, et al. Development of a health-related quality-of-life questionnaire (PCOSQ) for women with polycystic ovary syndrome (PCOS). J Clin Endocrin Metab, 1998; 83: 1976–87.
5. https://my.clevelandclinic.org/health/diseases/8316-polycystic-ovary-syndrome-pcos
6. Zawadzki JK, Dunaif A. Diagnostic criteria for polycystic ovary syndrome: toward a rational approach. In: Dunaif A, Givens JR, Haseline F, Merriam GR, eds. Polycystic Ovary Syndrome. Boston: Blackwell Scientific, 1990: 377-384.
7. Wolf WM, Wattick RA, Kinkade ON, Olfert MD. The current description and future need for multidisciplinary PCOS clinics. J Clin Med, 2018; 7: E395.
8. Kim JuH, Jung MH, Hong SeH, et al. Age-Adjusted Prevalence and Characteristics of Women with Polycystic Ovarian Syndrome in Korea: A Nationwide Population-Based Study (2010-2019). Yonsei Med J, 2022; 63(8): 794–798, doi: 10.3349/ymj.2022.63.8.794, indexed in Pubmed: 35914763.
9. Jabeen A, Yamini V, Rahman Amberina A, et al. Polycystic Ovarian Syndrome: Prevalence, Predisposing Factors, and Awareness Among Adolescent and Young Girls of South India. Cureus, 2022; 14(8): e27943, doi: 10.7759/cureus.27943, indexed in Pubmed: 36120281.
10. https://www.slideshare.net/slideshow/pcod-polycystic-ovarian-disease/50514741
11. https://www.slideshare.net/slideshow/pco-hirsutism/46878781
12. Burghen CA, Givens JR, Kitabchi AE. Correlation of hyperandrogenism with hyperinsulinemia in polycystic ovarian disease. J Clin Endocrinol Metab, 1980; 50: 113–116.
13. Zawadsky JK, Dunaif A. Polycystic ovary syndrome. In: Dunaif A, Givens JR, Haseltine FP, Merriam GR, editors. Polycystic Ovary Syndrome. Cambridge, MA: Blackwell Scientific, 1992; 377.
14. Zawadsky JK, Dunaif A. Polycystic ovary syndrome. In: Dunaif A, Givens JR, Haseltine FP, Merriam GR, editors. Polycystic Ovary Syndrome. Cambridge, MA: Blackwell Scientific, 1992; 377.

15. Jain S, Jain M, Shukla RC. Correlation of Clinical, Hormonal, Biochemical and Ultrasound Parameters Between Adult and Adolescent Polycystic Ovarian Syndrome: Adult and Adolescent PCOS. J Obstet Gynaecol India, 2022; 72(1): 274–280, doi: 10.1007/s13224-021-01557-z, indexed in Pubmed: 35928097.
16. Tsukui Y, Kitahara Y, Hasegawa Y, et al. Anti-Müllerian hormone levels in the diagnosis of adolescent polycystic ovarian syndrome: a systematic review and meta-analysis. Endocr J, 2022; 69(8): 897–906, doi: 10.1507/ endocrj.EJ22-0081, indexed in Pubmed: 35675999.
17. Tsai RY, Lee SH, Chan HL. The distribution of follicular units in the Chinese scalp: Implications for reconstruction of natural-appearing hairlines in orientals. Dermatol Surg, 2002; 28: 500-3.
18. Stein IF, Cohen MR. Surgical treatment of bilateral polycystic ovaries. Am J Obstet Gynecol, 1939; 38: 465.
19. Kiddy DS, Hamilton-Fairley D, Bush A, et al. Improvement in endocrine and ovarian function during dietary treatment of obese women with polycystic ovary syndrome. Clin Endocrinol (Oxf), 1992; 36: 105–111.
20. Derksen J, Moolenaar AJ, Van Seters AP, Kock DF. Semiquantitative assessment of hirsutism in Dutch women. Br J Dermatol, 1993; 128: 259-63.
21. Souter I, Sanchez LA, Perez M, Bartolucci AA, Azziz R. The prevalence of androgen excess among patients with minimal unwanted hair growth. Am J Obstet Gynecol, 2004; 191: 1914-20.
22. Sagsoz N, Kamaci M, Orbak Z. Body hair scores and total hair diameters in healthy women in the Kirikkale region of turkey. Yonsei Med J, 2004; 45: 483-91.
23. Lunde O, Grøttum P. Body hair growth in women: Normal or hirsute. Am J Phys Anthropol, 1984; 64: 307-13.
24. Knight JC. Regulatory polymorphisms underlying complex disease traits. J Mol Med (Berl), 2005; 83: 97-109.