International Journal of Studies in Natural and Medical Sciences
Volume 02 Issue 05, May, 2023
ISSN (E): 2949-8848
Scholarsdigest.org

Polycystic Ovary Syndrome (PCOS) and Adolescence: How to Deal With it? (Overview)

Kurbanova Zamira Shukhratovna
Bukhara State Medical Institute

Abstract
Polycystic ovary syndrome is a very complex syndrome with typical hormonal and metabolic features. In adolescent girls, this condition has certain characteristics that are shared with adult signs and symptoms, often making it difficult to diagnose. On the other hand, the treatment strategy aims to manage various aspects of this syndrome and is typically based on lifestyle/diet modification, possibly associated with the use of estrogens, antiandrogens, and insulin sensitizing agents. In this article, we will briefly review both the diagnosis and clinical approach to polycystic ovary syndrome in adolescence, which are still a matter of debate due to the specific hormonal environment of this critical period.

Keywords: adolescence, PCOS, insulin, estroprogestins, inositols, metformin.

Many years ago, Stein and Leventhal reported clinical cases of seven women suffering from a special condition characterized by a combination of amenorrhea, hirsutism, and polycystic ovaries [1], which was later recognized as polycystic ovary syndrome (PCOS) [2]. Subsequently, PCOS was considered the most common endocrinopathy in women of reproductive age, characterized by menstrual irregularities, increased androgen levels, and polycystic ovaries on ultrasound. In particular, in 2003 Rotterdam adopted a more detailed definition of this syndrome for adult women [3], defining PCOS as a condition characterized by at least two of the following characteristics: signs/symptoms of hyperandrogenism, anovulation, and polycystic ultrasonographic ovarian morphology. Insulin resistance with compensatory hyperinsulinemia, increased cardiometabolic risk, and endometrial cancer risk are potential comorbidities.

Both the definition and diagnosis of PCOS in adolescent girls can be difficult because some of the typical features of this syndrome can be detected during the physiological maturation stages of the hypothalamic-pituitary-ovarian axis. Thus, the diagnosis of PCOS in adolescent girls is usually more difficult than in older women [5,6] In fact, although the diagnostic criteria for this syndrome in adults were first described at a meeting of the National Institute of Child Health in 1990 and later refined at the

ESHRE/ASRM conference in Rotterdam in 2003 [14], specific diagnostic criteria are currently being demonstrated. The features of PCOS in adolescents are still controversial [4].

According to the Rotterdam criteria, the presence in the same subject of at least two of these three of the following characteristics can usually identify patients suffering from PCOS (after excluding other pathologies, i.e. hyperprolactinemia, Cushing's syndrome, hypothyroidism, virilizing tumors, etc:

• oligoamenorrhea.
• clinical and/or biochemical hyperandrogenism.
• morphologyofpolycysticovaries.

Interestingly, different PCOS phenotypes can be identified in this way:

-phenotype A = hyperandrogenism associated with ovulatory dysfunction and polycystic ovary morphology.
-phenotype B = hyperandrogenism associated solely with ovulatory dysfunction.
-phenotype C = hyperandrogenism and polycystic ovary morphology
-phenotype D = ovulatory dysfunction with polycystic ovary morphology [5].

However, this classification is less useful for defining PCOS in adolescence, since all three of the main criteria mentioned above are usually found during puberty. On the other hand, it is well known that it may take about 3 years after menarche for most girls to achieve a regular menstrual cycle. In addition, 41% of adolescent women have ovulatory cycles by the fourth gynecological year, despite the persistence of irregular menstruation [6].

Due to the current lack of adequate evidence, the most recent clinical guidelines suggest adjusting the timing of the assessment and diagnosis of PCOS by discussing with each patient, taking into account the typical diagnostic problems of her life stage and psychosocial aspects [7].

In particular, attention should be paid to girls with primary or secondary amenorrhea within 90 days at the age of 15–16 years and/or with persistent oligomenorrhea or irregular cycles within 3–4 years after menarche [8].

The definition of irregular menstruation consists of:

• 1 to 3 years after menarche, <21 days or >45 days.
• 3 years after menarche to perimenopause, <21 days or >35 days or less than eight cycles per year.
• From 1 year after menarche, >90 days for any one cycle.
• Primary amenorrhea at age 15 or >3 years after thelarche.

The approach to adolescents with PCOS always requires an accurate personal and family history along with an accurate clinical examination.

In particular, symptoms and signs of clinical hyperandrogenism, including severe acne, hair loss and hirsutism and/or hyperinsulinemia possibly associated with acanthosis

nigricans—clinical markers of hyperinsulinemia consisting of thickening of dark skin in skin folds—and/or frequent episodes of hypoglycemia. needs to be explored.

Hirsutism, characterized by excessive terminal male-pattern hair growth in women, is the most significant clinical sign of hyperandrogenism; it is usually measured using the Ferriman-Golway (mFG) scale, with a level ≥4–6 indicating pathological hirsutism, even though this limit may vary by ethnicity [9].

In addition, the spread of alopecia is usually assessed using the visual Ludwig scale; on the other hand, generally accepted visual indicators for assessing acne are still insufficient [7].

It should be emphasized that the severity of the clinical manifestations of hyperandrogenism can be varied, depending on many individual aspects, such as different peripheral sensitivity to androgens and/or their levels in the blood [3].

However, according to evidence-based guidelines, biochemical hyperandrogenism, usually defined as hyperandrogenemia, must be confirmed by dosing total and free testosterone using high-quality assays such as liquid chromatography-mass spectrometry (LC-MS) and extraction/chromatographic immunoassays, while while androstenedione and dehydroepiandrosterone sulfate (DHEAS) may be considered if total testosterone (TT) or free testosterone (FT) is not elevated. However, the dosage of FT may be hardly accurate and poorly reproducible [10].

It is important to remember that during puberty, insulin levels rise physiologically, followed by a decrease in sex hormone-binding globulin (SHBG) and an increase in free androgens, as well as a secondary stimulation of ovarian steroidogenesis; later in life, in subjects with PCOS, physiological hyperinsulinemia during adolescence can cause hyperandrogenism and ovulatory dysfunction.The routine determination of anti-Müllerian hormone (AMH) in the blood serum is not considered an important milestone in the diagnosis of PCOS, since its level is often elevated in women suffering from this syndrome. At present, AMH and cut-off analyzes do not allow a better study of young patients with PCOS [11].

Ultrasound evaluation of ovarian morphology is largely considered to be an adjunct to the clinical, hormonal, and metabolic analysis of PCOS in adult women as well as in adolescents. In addition, the frequent assessment of multifollicular ovaries and the usual difficulties in performing transvaginal examination may greatly reduce the value of ultrasound assessment [13].

Thus, a clear diagnosis of PCOS in adolescence should be based on the simultaneous identification of all three of the main diagnostic criteria of Rotterdam, i.e. oligoamenorrhea, hyperandrogenism and polycystic ovary morphology in any case after at least 2 years after menarche. Conversely, clinical observation should be addressed to those girls whose diagnosis remains unclear [14].

Metabolic syndrome, impaired glucose tolerance (IGT), and type 2 diabetes may be more common in adolescent girls with PCOS [[6], [7], [8]]. Thus, screening

for abnormalities in glucose tolerance and/or insulin response should be done with an oral glucose tolerance test (OGTT), measuring plasma glucose and insulin levels 2 hours after a standard oral glucose load (75 g) [12].

More specifically, since subjective sensitivity to glucose load must be assumed, reducing the area under the curve (AUC) of insulin during OGTT after any intervention (lifestyle, diet, insulin sensitizers) to reduce insulin resistance can help clinicians properly follow each patient and test treatment effects insulin resistance [13].

In addition, it is recommended that thyroid and adrenal function be assessed not only to rule out certain pathologies whose signs and symptoms may be shared with those of PCOS and thus potentially interfere with diagnosis, but also to identify some possible clinical associations.

With respect to the adrenal and gonadal axis, dosing of dehydroepiandrosterone sulfate (DHEAS), dehydroepiandrosterone (DHEA), 17-hydroxyprogesterone (17OHP), and cortisol may be useful to identify any possible interactions between ovarian and adrenal steroidogenic disorders, which have been clinically reported in about 25 % of cases. women with PCOS [7]. Moreover, 17OHP (at baseline and/or after ACTH stimulation) may be useful in diagnosing late 21-hydroxylase deficiency, usually first detected in adolescence [12].

In fact, in some cases, PCOS may be associated with a partial defect in this enzyme, producing an excess of adrenal hormones with androgenic activity, which can directly cause hirsutism, acne, oligo-amenorrhea, affecting the ovaries and/or peripheral levels. Genetic analysis to exclude the familiar tract in the development of a non-classical form of 21-hydroxylase deficiency should be offered to the patient based on personal and family history.

Treatment strategies for PCOS should be selected on an individual basis according to the general condition, metabolic and hormonal profile, and patient preferences, taking into account the benefit/risk balance of the various treatments available. Treatment goals should be to improve hormonal and metabolic status, quality of life, and long-term health.

Lifestyle and dietary changes, especially in overweight/obese patients, should be the basis of all treatments that involve increased physical activity (at least 60 minutes of moderate to vigorous physical activity per day at least 3 times per week), reduced total caloric intake (causing an energy deficit of 30% or 500–750 kcal/day) and/or dietary glycemic index [8].

Estroprogestins (EPs) are considered first-line drugs in the treatment of PCOS [11] and have been found to improve both menstrual irregularities and hyperandrogenism. EN can reduce ovarian androgen production, inhibit T binding to the androgen receptor (AR), reduce the activity of 5-alpha reductase (the enzyme that produces dihydrotestosterone-DHT- from T), and finally reduce androgen bioavailability; Interestingly, all ENs can increase hepatic production of sex hormone-binding globulin

(SHBG), thereby reducing free testosterone (FT) levels and also reducing peripheral hyperandrogenic manifestations (seborrhea, acne, hirsutism) [6].

Various EP combinations are currently available, including EP with estrogen and an antiandrogen progestin such as cyproterone acetate (CPA), dienogest (DNG), drospirenone (DRSP), chlormadinone acetate (CMA) [[2,9],[3] ,[3], while literature data have shown similar results in the treatment of hyperandrogenism with EPs containing an antiandrogenic progestin (cyproterone acetate-CPA) compared with a non-antiandrogenic progestin (desogestrel-DSG) in adolescent PCOS []; thus, at present, there is no clear superiority of one VP over others.

Regarding the metabolic impact of VP in adolescents with PCOS, glucose metabolism is potentially exacerbated by some EPs, as evidenced by significant changes in the HOMA index reported in a study of overweight adolescents (mean BMI > 25) with PCOS with both EE/CPA and with EE/DSG, and worse with EE/CPA [5].

Moreover, elevated glucose levels have been reported in obese patients with PCOS after an oral glucose tolerance test (OGTT) using EE/DSG [3,4] and EE/CPA [3,5]. On the other hand, in non-obese PCOS patients, EPs containing DSG or CPA did not alter glucose tolerance [36]; in addition, EE/DRSP did not change the response of glucose and insulin to OGTT in patients with PCOS [5].

These data suggest that the effect of EP on glucose and insulin metabolism may be related to both patient characteristics (obese and non-obese) and pharmacological composition.

Regarding the dose of EN used for adolescent PCOS, the lowest effective dose of estrogen (20–30 μg ethinyl estradiol or equivalent) and natural estrogen preparations (valerate or micronized estradiol) should be preferred based on their potential benefit/risk. contraindications, including overweight and obesity, which are common in PCOS [11].

If lifestyle modification and/or diet and/or EN do not adequately address hyperandrogenic manifestations, other drugs may be suggested, such as antiandrogen androgen receptor blockers (flutamide, spironolactone) and 5α-reductase inhibitors (finasteride). -. In particular, if EN and dermatological interventions do not adequately reduce hirsutism for 6 months or more, antiandrogens can be added, carefully assessing the benefit / risk ratio, since, as a rule, they (flutamide, finasteride) do not have specific indications for clinical use. . in women [7].

Furthermore, the combination of antiandrogens and EP may be a valid treatment option for androgen-associated alopecia in PCOS [2]. The use of antiandrogens alone may also be suggested for the treatment of androgen-mediated alopecia and hirsutism if EN is contraindicated or poorly tolerated; however, in this latter case, the combination of antiandrogens with an effective method of contraception is required in order to avoid potential undervirilization of the male fetus [].

Metformin, a powerful insulin sensitivity enhancer [4], can be used in combination with EP in women with PCOS to treat metabolic problems [3], first when EP and lifestyle changes do not achieve the desired beneficial effects. In particular, metformin can be added to EN in adolescents with PCOS and BMI ≥ 25 kg/m2. In addition, metformin itself can directly affect reproductive function. Numerous studies have demonstrated a moderate ability of metformin to positively influence the regularity of the menstrual cycle, acne, and hirsutism [8]

PCOS is a very complex syndrome in which hormonal and metabolic factors can coexist.

Diagnosis and/or follow-up of this syndrome in adolescent girls is difficult due to the overlap between the main features that are usually considered in the diagnosis in adult women and various characteristics observed at different stages of adolescence, such as menstrual irregularities, signs of hyperandrogenism (seborrhea, acne), weight gain and multifollicular appearance of the ovaries on ultrasound. The treatment strategy for adolescents with PCOS should be based on lifestyle and/or dietary changes, use of EP (plus antiandrogens as needed) and, if needed, insulin sensitizers such as inositols and metformin, depending on the individual, but mainly with a multidisciplinary approach.

Literature

1. Akhmedov F.K., Negmatullaeva M.N., Features of the state of central hemodynamics and hemostasis in pregnant women with preeclampsia of varying degrees and severity// New Day of Medicine. - 2020. - No. 1 (29) - S. 147-150.
2. Akhmedov F.K., Negmatullaeva M.N., Kurbanova Z.S.Modern views on the problem of preeclampsia - A new day in medicine, 2018– C.180-185
3. kholovaNodiraFazliddinovna.Diagnosis of reproductive health disorders in girls of early reproductive age // Electronic scientific journal "Biology and Integrative Medicine" No. 5 - September-October (52) 2021
4. Selma Feldman Witchel, Sharon E. Oberfield, Alexia S. Peña Polycystic ovary syndrome: pathophysiology, manifestations, and management with a focus on adolescent girls. J Endocrine Soc, 3 (August 8) (2019), pp. 1545–1573, 10.1210/js.2019-00078).
5. D. Dewailly, M. E. Lujan, E. Carmina, et al.The Definition and Significance of Polycystic Ovary Morphology: A Society Task Force Report on Androgen Excess and Polycystic Ovary Syndrome. Hum Reprod Update, 20(3)(2014), pp. 334–352.
6. E. Codner, C. Villarroel, F.C. Eizaguirre, P. Lopez, P. M. Merino, F. Pérez-Bravo and othersMorphology of polycystic ovaries in adolescents in the postmenarchal periodFertilSteril, 95 (2) (2011), pp. 702–706.e1–2.
7. B.C. Fauser, B.C. Tarlatzis, R.W. Rebar, etc.Consensus on Health Aspects of Women with Polycystic Ovarian Syndrome (PCOS): 3rd PCOS Consensus

Working Group sponsored by ESHRE/ASRM in AmsterdamFertilSteril, 97 (January (1)) (2012), pp. 28–38.e25, 10.1016/j.fertnstert.2011.09.024Epub 2011 Dec 6

8. F. Fruzzetti, D. Perini, V. Lazzarini and othersHyperandrogenemia affects the prevalence of metabolic syndrome disorders in adolescents with polycystic ovary syndrome. GynecolEndocrinol, 25 (2009), pp. 335-343.
9. E.B. Gur, M. Karadeniz, G.A. Turan. Fetal programming of polycystic ovary syndromeWorld J Diabetes, 6(July 10(7)(2015)), pp. 936–942, 10.4239
10. Shamsievna R. G. Modern Aspects of Studying the Features of Morphofunctional Characteristics of Testes under Various Factor Influences //Eurasian Scientific Herald. – 2022. – Т. 7. – С. 279-286
11. Sh R. G. Experimental modelling of traumatic brain injury in white rats //Тиббиётда янги кун. – 2021. – Т. 2. – №. 34. – С. 197-200.
12. Shamsievna, R. G. (2023). The Leading Mechanisms of the Pathophysiology of Traumatic Brain Injuries. *Scholastic: Journal of Natural and Medical Education*, *2*(3), 115–119.
13. Rakhimova G. New day in medicine //New day in medicine Учредители: Бухарский государственный медицинский институт, ООО" Новый день в медицине". – №. 2. – С. 197-200.
14. R.S. Legros, S.A. Arslanyan , D.A. Ehrmann and others.Diagnosis and Management of Polycystic Ovary Syndrome: Clinical Practice Guidelines of the Society of Endocrinologists. J ClinEndocrinolMetab, 98 (2013), pp. 4565-4592.
15. M. Forets, B. Gigas, L. Bertrand and others. Metformin: from mechanisms of action to therapyCellular Metabolism, 20 (2014), pp. 953–966.
16. M. Artani, M. F. Iftikhar, S. Khan. Effect of metformin on symptoms of polycystic ovary syndrome in women of reproductive ageCureus, 10 (25 (8) August) (2018) , p. e3203.
17. KurbanovaZ.Sh., Ikhtiyarova G.A., Rozikova D.K. - Anovulatory infertility and polycystic ovary syndrome // Tibbiyotdayangi kun 2 (30/2) 2020 pp. 159-165
18. KurbanovaZ.Sh., Ikhtiyarova G.A., Rozikova D.K. - Causes and methods of diagnosing endocrine infertility and the role of vitamin D in its correction // Tibbiyotdayangi kun 2 (30/2) 2020 pp. 34-38.