Original Study

Do Different Diagnostic Criteria Impact Polycystic Ovary Syndrome Diagnosis for Adolescents?

Sinem Akgül MD, PhD *, Yasemin Düzçeker MD, Nuray Kanbur MD, Orhan Derman MD

Division of Adolescent Medicine, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey

A B S T R A C T

Study Objective: Although early diagnosis of polycystic ovary syndrome (PCOS) in adolescents might allow for earlier treatment and prevention of chronic disorders, incorrect or premature diagnosis carries risks of unnecessary treatment and psychological distress. There is no consensus concerning which diagnostic criteria to use for adolescents and current criteria vary. The objective of this study was to determine whether using different diagnostic criteria will affect PCOS diagnosis in adolescents.

Design, Setting, and Participants: Fifty-two patients aged 13-18 years with at least 2 of the following criteria were included in the study: (1) oligomenorrhea or amenorrhea; (2) Clinical or biochemical hyperandrogenism; and (3) polycystic ovaries on ultrasonography. Patients were then categorized according to the 6 different criteria for PCOS. National Institutes of Health, Rotterdam criteria, Androgen Excess Society, Amsterdam criteria, Endocrine Society criteria, and the Pediatric Endocrine Society criteria. The characteristics of adolescents who were diagnosed with PCOS were also evaluated.

Interventions and Main Outcome Measures: Forty-one patients out of 52 (78.8%) received diagnosis with National Institutes of Health and Endocrine Society criteria, all with Rotterdam criteria, 45/52 (86.5%) with Androgen Excess Society criteria, 36/52 (69.2%) with Amsterdam criteria and 34/52 (65.4%) with the Pediatric Endocrine Society criteria.

Results and Conclusion: This study shows that the choice of guideline used does have a great effect on whether an adolescent received the PCOS diagnosis or not. For physicians using the broader criteria, care should be taken to ensure the patient does not receive diagnosis because of the physiological changes seen during puberty, which might mimic PCOS. For those using stricter criteria, close monitoring of patients who do not receive diagnosis is necessary to prevent chronic complications.

Key Words: Adolescents, Diagnostic criteria, Polycystic ovary syndrome

Introduction

Currently, there are different criteria proposed for the diagnosis of polycystic ovary syndrome (PCOS). Although all require the exclusion of other causes of hyperandrogenism, certain differences are found in each guideline and no definite consensus has been made concerning the diagnosis in adolescents.[1]

The first criteria were introduced in 1990 by the National Institutes of Health (NIH). The consensus reached by the NIH concluded that PCOS diagnosis could be made in a patient with clinical and/or biochemical hyperandrogenism associated with a menstrual irregularity.[2]

After the NIH criteria, the European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine criteria were developed, which are often called the Rotterdam criteria, this guideline includes polycystic ovary morphology (PCOM) on ultrasonography to the other 2 NIH criteria but allows for combination of any 2 of the 3 findings of hyperandrogenism, menstrual irregularity, and PCOM. These guidelines added 2 new phenotypes to those described by the NIH Consensus because women with regular menstrual cycles or those with no hyperandrogenism might receive diagnosis. So, according to the Rotterdam phenotypic application models, individuals with all Rotterdam diagnostic criteria (hyperandrogenism, chronic anovulation, and PCOM) are in group 1; with hyperandrogenism and chronic anovulation are in group 2; with hyperandrogenism and PCOM are in group 3; and with chronic anovulation and PCOM are in group 4.[3]

However, this application model, especially for the group of patients who do not have hyperandrogenism, led to significant controversy. Thus, in 2006 the Androgen Excess Society (AES) criteria were defined, the main difference stated was that diagnosis required the presence of hyperandrogenism, with the associated findings of either menstrual irregularity and/or PCOM.[4]

The diagnosis of PCOS during adolescence is difficult because many of the signs and symptoms of the syndrome are also normal findings of pubertal development.[5] It has been argued that using the diagnostic criteria for adults might cause overdiagnosis of the syndrome and none of the 3 guidelines described previously discussed the diagnosis in the adolescent population.[6] In 2012 at the European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine-sponsored PCOS consensus workshop held in Amsterdam, it was stated that criteria for the diagnosis of PCOS in adolescents differ from those used for adult women of reproductive age. These criteria argued

The authors indicate no conflicts of interest.

* *Address correspondence to:* Sinem Akgül, MD, PhD, Division of Adolescent Medicine, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara 06100, Turkey; Phone 0312-3051160

E-mail address: sinemhusnu@gmail.com (S. Akgül).

1083-3188/$ - see front matter
https://doi.org/10.1016/j.jpag.2017.12.002

that because physiological characteristics of adolescence might overlap with PCOS signs, to avoid overdiagnosis PCOS should require all 3 of the Rotterdam consensus and not just 2 of 3.[7] Just 1 year later the Endocrine Society (ES) clinical practice guideline for the diagnosis and treatment of PCOS was published. This guideline also devoted separate recommendations for adolescents. Again, the guidelines state that the diagnosis of PCOS in an adolescent girl is different from that of an adult and the diagnostic criteria are similar to that of the NIH criteria in which clinical and/or biochemical evidence of hyperandrogenism after exclusion of other pathologies and oligomenorrhea is required. The difference between the two being that clinical hyperandrogenism is defined with only hirsutism by the ES for adolescents whereas it includes acne and alopecia for NIH criteria. An important point made in this guideline is that they state ultrasonography should not be a criterion for adolescents because the Rotterdam ultrasound polycystic ovary criteria have not been validated for adolescents and the PCOM might be a feature of normal puberty that subsides with the onset of regular menstrual cycling.[8]

In 2015, the Pediatric Endocrine Society (PES) invited experts to define appropriate diagnostic criteria for the diagnosis of PCOS in adolescence.[9] Their consensus supported the criteria of the ES in that persistent hyperandrogenic oligoanovulatory menstrual abnormality on the basis of age- and stage-appropriate standards should be used, with some modification. Biochemical hyperandrogenism was defined as persistent testosterone elevation above adult norms rather than the other serum androgens. Clinical hyperandrogenism was defined as moderate-severe hirsutism rather than mild hirsutism or moderate-severe inflammatory acne vulgaris. Another difference these criteria added was that the criteria for evidence of oligoanovulation was defined as abnormal uterine bleeding pattern for age or gynecologic age with persistent symptoms for 1-2 years. Again, PCOM was not recommended as a diagnostic criterion by the PES.

With all of these different guidelines being used for PCOS definition, where does this leave the clinician working with adolescents? PCOS is not only frequently encountered but also an important cause of morbidity so it is recommended that the disorder is diagnosed early,[10] but will trying to diagnose the disorder early on cause over- or premature diagnosis of the disorder because many findings might be transitory?[6]

The aim of this report was to evaluate whether a PCOS diagnosis would change according to the criteria used and to evaluate characteristics of adolescents who were diagnosed with PCOS.

Materials and Methods

A retrospective chart evaluation was conducted and female patients aged 13-18 years who applied to Hacettepe University Ihsan Doğramacı Children's Hospital, Division of Adolescent Medicine between January and July 2016 with at least 2 of the following criteria were included in the study: (1) Oligomenorrhea or amenorrhea; (2) clinical or biochemical hyperandrogenism; and (3) polycystic ovaries on ultrasound scan.

Oligomenorrhea was defined as the absence of menstruation over 45 days and amenorrhea as no menstrual bleeding for 6 months. Patients were only eligible to enroll 2 years after menarche. Hyperandrogenism was defined when total testosterone was greater than 50 ng/mL biochemically, and the score was at or greater than 8 according to m-Ferriman-Gallwey (mFG) classification clinically.[11] A total score of 8-15 was used to define mild hirsutism, 16-24 moderate hirsutism, and greater than 24 severe hirsutism.[5] Moderate to severe acne was noted for clinical hyperandrogenism.

Exclusion criteria were any other cause for oligomenorrhea or hyperandrogenism such as nonclassic adrenal hyperplasia, androgen secreting neoplasms, Cushing syndrome, thyroid dysfunction, and hyperprolactinemia, any patients with a history of androgenic/anabolic drug or contraceptive use, or any patient who refused participation in the study.

Systemic physical examination was performed on all patients and the presence of acne, acanthosis nigricans, male pattern hair loss, and virilization were recorded. Pubertal stages of patients were performed according to the Marshall-Tanner method.[12] Measurements of weight (kilograms) were obtained using electronic scales (Seca 220; Hamburg, Germany), and measurements of height (centimeters) were obtained using the Harpenden stadiometer. Measurements were evaluated according to normal values of Turkish children, which were modified according to age and gender. Body mass index was calculated by using the body weight in kilograms divided by the height in meters squared formula. Children within the 85th-95th percentiles were accepted as overweight, whereas at and greater than the 95th percentile was accepted as obese.[13]

The laboratory evaluation included the total blood count, liver and kidney function tests, lipid profile, fasting glucose, fasting insulin level, Insulin Resistance Homeostasis Model of Assessment (IRHOMA) values, estrogen, total testosterone, sex hormone binding globulin, dehydroepiandrosterone sulfate, androstenedione, 17-hydroxy-progesterone, follicle-stimulating hormone, luteinizing hormone, prolactin levels, free androgen index, and thyroid function tests.

Blood samples for laboratory evaluations were drawn during early follicular phase (on day 2-3 of the menstrual cycle) in patients with menses. For patients with amenorrhea blood was drawn on the day of clinical examination after a 12-hour fasting at 8:00 AM.

Serum follicle-stimulating hormone, luteinizing hormone, estradiol, prolactin, thyrotropin, free triodothyronine and free thyroxine levels were measured using the 2-step chemiluminescence microparticle immunoassay method. Sex hormone binding globulin and 17-OH progesterone were tested using immunoradiometric assay. Serum dehydroepiandrosterone sulfate and total testosterone levels were determined using solid phase chemiluminescence immunoassay. Glucose level was measured using the glucose hexokinase method; total cholesterol was studied enzymatically using the oxidase method; high-density lipoprotein cholesterol was studied using the direct non-immunological method; fasting insulin was studied using the radioimmunoassay method. Fasting insulin and IRHOMA values were used in the evaluation of insulin