Original Study

The Value of Prostate-Specific Antigen in Diagnosis of Polycystic Ovarian Syndrome in Adolescent Girls

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A B S T R A C T

Study Objective: This study was designed to evaluate and compare the serum total prostate-specific antigen (PSA) levels in adolescent girls in with and without polycystic ovarian syndrome (PCOS) to show whether evaluation of PSA levels have a diagnostic benefit over existing diagnostic criteria.
Design: Case-control study.
Setting: A territory referral center.
Participants: A total of 89 (15-19 years) nonobese (body mass index, 18-24.9) adolescents with PCOS (n = 42) and controls without PCOS (n = 47) were enrolled in the study.
Interventions: Pathophysiological features of PCOS and serum total PSA levels were determined at the time of study enrollment.
Main Outcome Measures: Determination, comparison, and diagnostic performance of serum total PSA levels in diagnosis of PCOS in adolescent girls were the main outcome measures of the study.
Results: The serum total PSA levels of adolescents with PCOS were detected to be higher than for control participants (0.63 ± 1.38 ng/mL vs 0.48 ± 0.95 ng/mL) without meeting statistical significance (P = .923). There was a correlation between total PSA levels and indices of insulin resistance like the homeostasis insulin resistance model (r = 0.414; P = .010). The serum total PSA level was not a discriminative parameter for diagnosis of PCOS in adolescent girls (area under the curve, 0.559; P = .476).
Conclusion: The serum total PSA level was not a predictor of PCOS in adolescent girls. This finding might be related to the extemporal nature of tissues capable of PSA production and lack of sufficient exposure interval to hyperandrogenemia, rather than lack of stimulatory relationship between serum androgens.
Key Words: Adolescence, Hyperandrogenemia, Hyperinsulinism, Insulin resistance, PCOS, PSA

Introduction

Diagnosis of polycystic ovarian syndrome (PCOS) in adolescence is still a challenging issue in gynecology practice because of the physiological and anatomical changes encountered during this period. According to criteria proposed by the National Institutes of Health, PCOS has been defined as the presence of oligo-ovulation/anovulation and clinical or biochemical hyperandrogenism that cannot be explained by other associated diseases.[1] Additionally, in the absence of other causes, the same phenomenon has been defined as the presence of at least 2 of the following 3 criteria: polycystic ovarian appearance in the ovaries, oligoanovulation, and clinical or biochemical hyperandrogenism according to the consensus statement declared at Rotterdam in 2003.[2] First of all, it is challenging to distinguish between the physiological anovulation of puberty and anovulation related to PCOS.[3] Half of the cycles are anovulatory in the very first years after menarche.[4] Second, determining the presence of polycystic ovarian appearance is indeed a challenge because of the frequency of multicystic ovaries encountered as a normal variant in adolescence. Additionally, the sensitivity of ultrasound is diminished when performed through the abdominal route, which is generally the preferred methodology for adolescent girls.[5] Finally, slight acne and hirsutism might be encountered as a common sign of functional hyperandrogenism in adolescence as an overlapping symptom of the syndrome as well as physiological changes during puberty.[6] Consequently, the presence of PCOS should be suspected in any adolescent with hirsutism or its equivalent, menstrual irregularities, or obesity.

Prostate-specific antigen (PSA), a serine protease and a well known tumor marker of prostate cancer, is produced under the regulation of the stimulatory effects of androgens, progestins, glucocorticoids, and inhibitory effects of estrogens.[7,8] It has previously been shown that PCOS, a very well known hyperandrogenic state, is associated with higher levels of PSA.[9] PSA has also been identified as a potential new marker of hyperandrogenism in hirsute women.[9] However, some have theorized that PSA might serve as a useful marker or might even represent a diagnostic criterion for hyperandrogenemia-related diseases such as PCOS. Depending on the gathered data, we hypothesize that the detection of increased levels of PSA might help to facilitate diagnosis of PCOS in adolescent girls by overcoming previously described diagnostic challenges.

The authors indicate no conflicts of interest.

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A brief understanding of the existing literature is helpful. The guidelines proposed by the Rotterdam European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine sponsored PCOS consensus workshop group have resulted in a more uniform diagnosis of PCOS in adolescence, but the commonly used biochemical markers of hyperandrogenemia and suggested vaginal ultrasound measurements still appear to yield highly variable diagnostic performance.[2] Therefore, this study was designed to evaluate and compare serum PSA levels in adolescent girls with and without PCOS to determine whether evaluation of PSA levels results in a diagnostic gain over existing diagnostic criteria. Additionally, possible correlations between PSA and several clinical and biochemical features of PCOS, such as Ferriman-Gallwey score (FGS), serum levels of androgens and insulin, and indices of insulin resistance, such as the homeostasis insulin resistance model (HOMA-IR) and glucose insulin ratio (GIR), were evaluated.

Materials and Methods

The present study was approved by the Ethical Committee of Ankara Zekai Tahir Burak Women's Health, Research and Education Hospital and was conducted in accordance with the Declaration of Helsinki. Written and verbal informed consent was obtained from all study participants, as well as from their parents.

Study Population

The study population comprised a total of 89 (between 15 and 19 years of age) nonobese (body mass index [BMI], 18-24.9) adolescents with PCOS (n = 42), diagnosed according to the recent European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine proposal, with the requisite presence of all 3 of the criteria declared in the consensus statement of Rotterdam: oligo- or anovulation, clinical and biochemical signs of hyperandrogenism, and polycystic ovaries,[2] as well as adolescents without PCOS (n = 47). Participants, who received care at the outpatient adolescent clinic of Ankara Zekai Tahir Burak Women's Health, Research and Education Hospital, were prospectively enrolled in this case-control study between March 2014 and August 2014.

The participants were assigned through enrollment to either the study group or the control group. The participants enrolled in the control group had normal menstrual cycles, with no evidence of hyperandrogenism, including an FGS[10] of less than 8 and normal ovaries in appearance on abdominal ultrasonographic evaluation. Participants who had systemic disorders, such as diabetes, thyroid disease, adrenal, hepatic, or cardiovascular disorders, and who were receiving therapies that could affect carbohydrate and lipid metabolism, such as corticosteroids, statins, aspirin, and oral contraceptives, were excluded from the study. Additionally, patients diagnosed with hyperprolactinemia, Cushing syndrome, or congenital adrenal hyperplasia, benign or malign breast diseases, and pregnancy were excluded from the study.

Clinical or biochemical hyperandrogenism was detected if the FGS was greater than 8, acne was present, and serum concentrations of free testosterone (free-T) greater than 3.6 ng/mL and/or a dehydroepiandrosterone sulfate (DHEA-S) level greater than 9.7 mmol/L (357.4 ng/dL) were detected.[11] All participants had a menarche age of at least 3 years. Oligo- or amenorrhea was defined as the presence of a cycle length in excess of 45 days or less than 8 spontaneous menstrual cycles per year, or the absence of menstruation for more than 3 months.[12] The ovaries were considered polycystic using transabdominal ultrasonography when increased stromal echogenicity was peripherally surrounded by more than 12 follicles with a diameter of 2-8 mm or an ovarian volume of greater than 10 cm^3 was detected on each of the ovaries.[13] Transabdominal ultrasonography was performed by the same investigator (A.T.) for all participants. All ultrasonographic examinations were performed using a 3.5-MHz transabdominal convex transducer (SSD 1000; Aloka, Tokyo, Japan).

Demographic, physical, and clinical characteristics of the patients were defined at the time of study enrollment. All anthropometric measurements were performed on all participants wearing light clothes without shoes. BMI was calculated by dividing the weight of patients in kilograms by their square of height in meters. Waist circumference (WC) was measured at the midpoint between the last rib and hip, whereas hip circumference was measured at the level of the greater trochanter. Waist-to-hip ratio (WHR) was calculated by dividing WC by hip circumference. The BMIs, WHRs, acne status,[14] and FGSs[10] were assessed by a single investigator (A.T.) for all participants, as previously described.

Laboratory Studies

All laboratory studies were performed at the early follicular phase on day 3 of a spontaneous or progesterone-induced menstrual cycle for each participant after an overnight fasting period of 8-12 hours in the early morning (8-10 AM). Biochemical evaluation consisted of the following: fasting glucose and insulin, C-reactive protein, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol, free-T, 17-hydroxyprogesterone, DHEA-S, prolactin, and thyroid stimulating hormone.

Serum biochemistry, including total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides, was determined using an AU680 Chemistry System (Beckman Coulter) using appropriate reagents. Serum levels of hormones, including FSH, LH, estradiol, DHEA-S, and insulin, were measured using the UniCel DxI 800 Immunoassay System (Beckman Coulter). Serum 17-hydroxyprogesterone and free-T levels were measured using radioimmunoassay. C-reactive protein was measured via a nephelometric method with the use of the BN II System (Siemens, Erlangen, Germany). Insulin resistance was calculated using the HOMA-IR, which was computed with the following formula: HOMA-IR = (fasting insulin [mIU/mL] × glucose [mg/dL])/405.

Total serum PSA levels were measured using a sensitive direct immunoenzymatic determination method (DCM057-5; DiaMetra). The minimum concentration level of assay