

Polycystic Ovary Syndrome As A Predictor Of Metabolic Syndrome In Women Of Reproductive Age

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Relevance. Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age. The prevalence rates of PCOS depend on the diagnostic criteria used and the characteristics of the population sample, and in the general population of women of reproductive age, the prevalence of the syndrome ranges from 6-9% to 19.9% [1,2]. According to modern criteria adopted by the consensus in Rotterdam, then systematically updated by ESHRE / ASRM (2014), the presence of two of the three criteria in a patient simultaneously allows to diagnose PCOS if other pathological conditions are excluded (thyroid pathology, congenital adrenal hyperplasia, adrenogenitalsyndrome, androgen-secreting tumors, Itsenko-Cushing syndrome). Modern international diagnostic criteria include the following signs: 1) signs of polycystic ovaries according to information from pelvic ultrasound investigation (the presence of more than 10 follicles in each ovary); 2) oligo-anovulation; 3) clinical (presence of hirsutism) or biochemical (increased androgen levels) development of ovarian hyperandrogenism [3, 4].

Polycystic ovary syndrome is closely related to many diseases, including metabolic syndrome. Although insulin resistance is an important risk factor for metabolic syndrome and other diseases associated with PCOS, hyperandrogenismmay also be an independent risk factor for type 2 diabetes, obesity, cardiovascular disease (CVD), and metabolic syndrome in female patients.

Obesity is the most common symptom in PCOS patients (33-88%), which has a large impact on fertility and can lead to adverse effects such as menstrual irregularities, anovulation, infertility and abortion. Therefore, weight management in early PCOS is essential to improve fertility and quality of life.

Hyperandrogenism plays a decisive role in abdominal obesity in obese women during adolescence, adulthood and menopause [5]. Although some studies have shown a negative association between plasma androgen levels (A4, DHEA and DHEAS) and obesity [6,7]. But the mechanism of how androgens affect fat cells in women is poorly understood. A number of observations show that among obese women with PCOS, metabolic disorders associated with insulin resistance and obesity, in many cases, play a more important role in the mechanism of anovulation in PCOS than excess androgens. In recent years, it has been established that in PCOS there is a frequent combination of hyperandrogenism and insulin resistance. With insulin resistance, there is a decrease in the response of insulin-sensitive tissues to the hormone insulin with its sufficient level in the blood. Insulin resistance is found in 30–70% of

patients with PCOS who are overweight or obese, and in patients with normal body weight it occurs in 20–25% of cases.

The above facts, as well as our own observations, prompted us to analyze the studied women of fertile age with impaired reproductive system against the background of overweight and obesity.

Considering the above, **the aim of this study** was to identify the relationship between insulin resistance and reproductive disorders in women with overweight and obesity.

Material and research methods. The study included 123 women with clinical development of HA and impaired reproductive function, who consulted the consultative clinic of the RSSPMC of Obstetrics and Gynecology of the Ministry of Health of the Republic of Uzbekistan. The criteria for inclusion in the main group were: age of women from 18 to 35 years (average age was 25.8 \pm 3.28 years), absence of pregnancy, body mass index over 25 kg / m2.

Exclusion criteria from the main group: type 1 and 2 diabetes, pituitary tumors, hypogonadotropichypogonadism, congenital adrenal hyperplasia, hypothyroidism, severe somatic pathology.

All patients who applied for the consultation underwent:

1. Collection of anamnestic information.

2. Measurement of anthropometric indicators (height, weight, waist and hip circumference) and assessment of body hair growth using the Ferriman-Hallway scale.

3. Body mass index was calculated using the formula: BMI = weight (kg) / height (m²).

4. Ultrasound examination of the uterus and ovaries, as well as the thyroid gland.

5. Hormonal examination (prolactin, LH, FSH, TSH, Anti-TPO, T4sv., 17-OH-progesterone, DHEA-122C, insulin).

6. Plasma glucose was measured using the hexokinase method using standard equipment and methods (Roche Diagnostics with Cobas Integra kits, Basel, Switzerland).

7. The HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) index was calculated using the following formula:

HOMA = (fasting plasma glucose (mmol / L) * fasting insulin (μ IU / ml)) / 22.5 (normally less than 2.7).

Ultrasound examination was carried out on a modern ultrasound apparatus of an expert class MindrayDC-70 with a sensor sensitivity of 7.5 MHz, preference was given to transvaginal access. Regularly menstruating patients were examined in the early follicular phase (3-5 days of the cycle), and patients with opso- / amenorrhea - on the day of consultation or on the 3-5th day of induced bleeding after a gestagenic test. The follicles were counted both in the longitudinal, transverse and anteroposterior sections of the ovaries, the volume of the ovaries, the average size of the follicles measured in three sections and the index of the ratio of the stromal area to the area of the ovary.

The hormonal study was carried out on an immunoassay analyzer Mindray 96 MR-96A China 2014.

Statistical processing of the research results was carried out using generally accepted methods using a personal computer, Microsoft Word 2016, Microsoft Excel programs.

Results and discussion. At the first stage of the research, the anamnesis of the disease, indicators of objective and anthropometric studies were analyzed, an ultrasound examination of the uterus and ovaries, and the thyroid gland was carried out. The age of the examined women varied from 18 to 35 years, which averaged 25.8 ± 3.28 years. The main complaints during treatment were menstrual irregularities in the form of oligo- or opsomenorrhea, inabilityto get pregnant, acne, excessive hair growth, overweight, hair loss, galactorrhea, headaches. Clinical signs of menstrual irregularities were detected in all studied women in the form of oligo- and opsomenorrhea, hyperpolymenorrhea - in 38 (31%) women, chronic anovulation - in 76 (61.78%) and amenorrhea in 15 (12, 2%) women under study.

During clinical examination, all examined patients had hirsutism (mean hirsutism was 17.2 ± 0.3 points on the Ferriman-Hallway scale, of which mild hirsutism prevailed - 81%, moderate hirsutism was found in 10% of the participants, marked hirsutism was found in 9% of patients. Other clinical developments of hyperandrogenism were also noted, such as acne was found in 48% of patients, negroidacanthosis in almost 20% of women, while alopecia was found in 11.4% of cases.

Determination of the body mass index in the surveyed women indicated the presence of overweight and obesity in more than half of the patients, which is one of the signs of metabolic syndrome. Of the total number of examined patients, in more than half of 53% of cases, overweight was detected, with an average BMI of 27.45 \pm 0.18 kg / m², obesity of the 1st degree was recorded in 19% of women with an average BMI of 32.82 \pm 0.52 kg / m², 25% of women had a normal body mass index with an average of 23.11 \pm 0.14 kg / m², and 3% of women in the study had a body weight deficit with an average BMI of 18.1 \pm 0.11kg / m².

The average age of the onset of menarche was 12.5 ± 2.8 years, of which the majority had an earlier onset of menarche at 10-11 years old - in 11 patients (9%) and at 12-13 years old in 80 patients (65%), in 13 -14 years old - at 32 (26%)

Female infertility was diagnosed in 78 surveyed women, of which 61 cases (78.2%) of primary infertility and secondary infertility occurred in 17 women (21.8%). The average duration of infertility is 4.01 ± 0.18 years.

Ultrasound examination revealed an increase in the volume of the ovaries due to the hyperechoic stroma, the average volume of enlarged ovaries varied from 14.07 ± 0.4 cm3 to 17.3 ± 0.7 cm3 (normal is 8.6 ± 0.3 cm3) with many (from 9 to 11) follicles with a diameter of 2-9 mm and with a predominance of 2-4 mm over 5-9 mm in diameter, located on the periphery of the ovaries. The total area of the stroma was 2.4 ± 0.6 cm2.

The hormonal study of patients revealed an increase in the level of LH (on average, $21.4 \pm 1.0 \text{ mIU} / \text{mI}$, while the reference values in the follicular phase are 0.9-15 mIU / mI). In 78% of women, the LH / FSH ratio was 3.1. In most cases, in the women under study, the concentration of prolactin in the blood was normal and averaged 407.8 ± 228.4 mMU / mI.

In our study, there is a moderate increase in the concentration of free testosterone, for example, in almost 64% of patients, the level of free testosterone averaged 5.7 \pm 0.3 ng / ml (laboratory reference values 0-4.1 ng / ml), while the concentration of DHEA -C in blood in 29% of the surveyed women showed higher than the standard values and averaged 5.8+ 2.95 µg / ml with reference values 0.8-3.9 µg / ml, and in the rest of the study patients did not exceed the standard values.

In women with overweight <30 kg / m2, the HOMA index was 3.47 ± 1.37 , and in obese women (BMI> 30 kg / m2) - 4.5 ± 2.03 , which indicates the development of IR. In the control group, this indicator was 2.56 ± 1.28 . Classic studies by Mitchell and Rogers showed that obesity is 3 times more likely to be associated with menstrual irregularities compared to women whose body weight is within normal limits. In women of reproductive age with overweight and obesity, the severity of IR was directly correlated with the severity of obesity, so if with a BMI <30 kg / m2 the HOMA index was 3.47 ± 1.37 , with a BMI> 30 kg / m2 this indicator on average was 4.5 ± 2.03 .

Conclusion. Thus, the dependence of insulin resistance indicators in women on BMI indicators was established, which indirectly indicates the presence of metabolic syndrome in these women. In connection with the above, it is advisable for all women of fertile age with overweight and obesity, regardless of the types of reproductive disorders with an increased level of the HOMA index, to monitor BMI indicators and take measures aimed at maintaining an ideal weight and reducing associated comorbidities.

Literature

- 1. Rosenfield DA. The RL, Ehrmann pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocr Rev. 2016;37(5):467-520.
- 2. Burger HG. Androgen production in women. FertilSteril. 2002;77:3-5.
- 3. Rotterdam ESHRE/ASRM-Sponsored ConsensusWorkshop Group. (2004). Revised 2003 consensus ondiagnostic criteria and long-term health risks related to polycystic ovary syndrome. Hum. Reprod., 19 (1), 41-47.
- FP, 4. Zawadzki J, Duniaf Α, Givens JR, Haseltine Merriam GR. (1992). Polycystic syndrome. Blackwell ovary Scientific Publications, 377-384.
- 5. Reinehr Τ, Kulle Α, Rothermel J, et al. Longitudinal analyses of the steroid metabolome in obese PCOS girls with weight loss. Endocr Connect. 2017;6(4):213-224.
- 6. Moran C, Arriaga M, Arechavaleta-Velasco F, Moran S. Adrenal androgen excess and body mass index in polycystic ovary syndrome. J ClinEndocrinolMetab. 2015;100:c9999.
- 7. Pasquali R, Oriolo C. Obesity and androgens in women. Front Horm Res. 2019;53:120-134.1836.