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Original Articles



Clinical manifestations of polycystic ovary syndrome: a modern view

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ABSTRACT

INTRODUCTION: Polycystic ovary syndrome (PCOS) is one of the urgent problems of gynecological endocrinology. The main signs of PCOS include a violation of menstrual and/or ovulatory function and clinical and/or biochemical hyperandrogenism, as well as polycystic ovarian morphology according to the ultrasound results. PCOS leads to infertility, obesity, and cardiovascular system diseases. PCOS is an important symptom complex in the diagnosis, which directly affects the reproductive function of females, hence the percentage of fertility. This study aimed to analyze the features of clinical, laboratory, and instrumental parameters in females with a previously established PCOS diagnosis referred for surgical treatment. The obtained results were studied from the point of view of the clinical guidelines of the American Society for Reproductive Medicine and the European Society of Human Reproduction and Embryology (2003), International PCOS Network (2018), and the Ministry of Health of the Russian Federation (2021).

MATERIALS AND METHODS: The study included 121 females who were admitted to hospitals in Moscow for surgical treatment. Among the gynecological surgical hospitals, the following medical institutions were allocated: the city clinical hospital, the research center, and the commercial clinic we conditionally divided into three levels.

The city clinical hospital had 54 females (1st group) aged 21–37 years, the research center with 48 females (2nd group) aged 22–42 years, and the commercial clinic with 19 females (3rd group) aged 25–41. Before the ovarian surgery for PCOS, all patients underwent an additional examination, including the collection of anamnesis, particularly, features of menstrual and generative function, anthropometric indicators, body weight, and height study. Based on these parameters, the body mass index (BMI) was calculated, the clinical signs of hyperandrogenism (acne, excessive hair growth on the body and face, and the degree of hirsutism) were assessed, and the hormonal profile was determined to detect biochemical hyperandrogenism (free testosterone). Additionally, the level of glucose and insulin in the blood plasma was determined in all patients, and a pelvic ultrasound examination (ultrasound) was performed.

RESULTS: Menstrual irregularities were revealed, of which complaints were presented by a total of 49.5% of patients. The results of the preliminary selection of patients with PCOS for surgical treatment revealed that 108 (89.2%) had primary and secondary infertility, of whom 64 (52.9%) had BMI within the normative values, 29 (23.9%) were overweight, and 25 (20.6%) were obese. Clinical manifestations of hyperandrogenism were present in 61 (50.4%) patients included in the study. The level of free testosterone above the normative values (>2.85 pg/ml) was diagnosed only in 9 (7.4%) patients out of 121 who are included in the study. Additionally, this parameter was within the upper limit of the norm (average value of 2.78 ± 0.36 pg/ml) in 112 females but was combined with clinical manifestations of hyperandrogenism. Black acanthosis was noted in 6 (5.0%) patients with free testosterone levels in 3.01–3.64 pg/ml. Increased blood glucose levels were combined with obesity in 3 (5.5%) patients of 1st group and 1 (2.1%) in 2nd group. Insulin levels significantly exceeded the upper limit of the norm in 6 (5.0%) patients. The ultrasound result in all patients ($n=121$) revealed the presence of echographic signs of PCOS in PCOS was confirmed by ultrasound in 54 females in 1st group, 48 females in 2nd group, and 19 females in 3rd group.

CONCLUSION: Our results suggest an unreasonably broad interpretation of PCOS diagnosis. Therefore, PCOS diagnosis should be primarily remembered as a diagnosis-exception. Only repeated, extended, thorough, and comprehensive examination of patients with a presumed PCOS diagnosis will allow you to better navigate the individual characteristics of patients and offer adequate methods for correcting the symptom complex to improve the overall health, fertility, and quality of life.

Keywords: polycystic ovary syndrome; menstrual disorders; hyperandrogenism; infertility; body mass index; insulin; free testosterone; ultrasound signs of polycystic ovaries.

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Оригинальное исследование

Клинические проявления синдрома поликистозных яичников: современный взгляд на проблему

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АННОТАЦИЯ

Введение. Синдром поликистозных яичников (СПКЯ) — одна из актуальных проблем гинекологической эндокринологии. К основным признакам СПКЯ относятся нарушение менструальной и/или овуляторной функции, клиническая и/или биохимическая гиперандрогения, а также поликистозная морфология яичников по результатам УЗИ. СПКЯ приводит к бесплодию, ожирению, заболеваниям сердечно-сосудистой системы. СПКЯ — это важный в диагностике симптомокомплекс, непосредственно влияющий на репродуктивную функцию женщин, а значит, и на уровень рождаемости.

Цель работы — проанализировать клиническую трактовку специалистами диагноза СПКЯ.

Материалы и методы. В исследование включили 121 женщину, поступившую для хирургического лечения в стационары Москвы: в городскую клиническую больницу — 54 женщины (1-я группа) в возрасте 21–37 лет, в научно-исследовательский центр — 48 женщин (2-я группа) в возрасте 22–42 лет, в коммерческую клинику — 19 женщин (3-я группа) в возрасте 25–41 года. До хирургического вмешательства на яичниках по поводу СПКЯ всем пациенткам проводили дополнительное обследование, включающее сбор анамнеза (особенности менструальной и генеративной функции), изучение антропометрических показателей — масса тела и рост; на основании этих параметров вычисляли индекс массы тела (ИМТ), проводили оценку клинических признаков гиперандрогении (акне, избыточный рост волос на лице и теле), оценку степени гирсутизма и определение гормонального профиля для выявления биохимической гиперандрогении (уровень свободного тестостерона). Кроме того, у всех пациенток определяли содержание глюкозы и инсулина в плазме крови, проводили ультразвуковое исследование (УЗИ) органов малого таза.

Результаты. Выявлены нарушения менструального цикла, жалобы на которые предъявляли суммарно 49,5% пациенток. Согласно результатам предварительного отбора пациенток с СПКЯ для хирургического лечения, у 108 (89,2%) из них отмечено первичное и вторичное бесплодие. Среди обследованных пациенток ИМТ в пределах нормативных значений имели 64 (52,9%) пациентки, 29 (23,9%) — избыточную массу тела, а 25 (20,6%) — ожирение. Клинические проявления гиперандрогении присутствовали у 61 (50,4%) пациентки, включённой в исследование. Уровень свободного тестостерона выше нормативных значений ($>2,85$ пг/мл) диагностирован только у 9 (7,4%) пациенток из числа включённых в исследование. У 112 женщин данный параметр находился в пределах верхней границы нормы (среднее значение $2,78 \pm 0,36$ пг/мл), однако сочетался с клиническими проявлениями гиперандрогении. Чёрный акантоз отмечен у 6 (5,0%) пациенток, имеющих уровень свободного тестостерона в пределах $3,01$ – $3,64$ пг/мл. Повышение уровня глюкозы в крови сочеталось с ожирением у 3 (5,5%) пациенток 1-й группы и у 1 (2,1%) пациентки 2-й группы. У 6 (5,0%) пациенток уровень инсулина существенно превышал верхнюю границу нормы. В результате УЗИ у всех пациенток ($n=121$), включённых в исследование, выявлено наличие эхографических признаков СПКЯ: в 1-й группе СПКЯ подтвердился по УЗИ у 54 женщин, во 2-й группе у 48 женщин, в 3-й группе у 19 женщин.

Заключение. Полученные нами результаты позволяют предположить неоправданно широкую трактовку диагноза СПКЯ. В связи с этим следует помнить, что диагноз СПКЯ — это диагноз-исключение. Только тщательное и всестороннее обследование пациенток с предполагаемым диагнозом СПКЯ позволит лучше ориентироваться в индивидуальных особенностях пациенток и предлагать адекватные методы коррекции симптомокомплекса для улучшения здоровья и повышения качества жизни.

Ключевые слова: синдром поликистозных яичников; нарушения менструального цикла; гиперандрогения; бесплодие; индекс массы тела; инсулин; свободный тестостерон; УЗИ-признаки поликистоза яичников.

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INTRODUCTION

Polycystic ovary syndrome (PCOS), also known as Stein–Leventhal syndrome, is a polyendocrine syndrome presenting with dysfunction of the ovaries (absence or irregularity of ovulation and increased secretion of androgens and estrogens), pancreas (hypersecretion of insulin), adrenal cortex (hypersecretion of adrenal androgens), hypothalamus, and pituitary gland [1].

The prevalence of PCOS among women of reproductive age ranges from 6% to 20% [2]. The clinical manifestations of PCOS are extremely diverse and are characterized by a combination of clinical, biochemical, and morphological signs, most of which persist in patients throughout their lives.

In clinical practice, the two most common definitions of PCOS are used. The first was formulated in 1990 by the consensus of an expert commission of the American National Institute of Health. According to this definition, the diagnosis of PCOS should be made in a patient with the simultaneous presence of symptoms of excessive activity or excessive secretion of androgens (clinical and/or biochemical) and oligoovulation or anovulation. It should be noted that, in this case, other causes of polycystic ovaries must be ruled out.

The second definition was formulated in 2003 in Rotterdam by a consensus of European experts [3]. According to the Rotterdam agreement, diagnosis of PCOS can be made if a patient has any two of the following symptoms at the same time:

- 1) symptoms of excessive activity or excessive secretion of androgens (clinical or biochemical),
- 2) oligoovulation or anovulation, and
- 3) polycystic ovaries on abdominal ultrasound (US).

Thus, a simple pairwise combination of signs can be transformed into a diagnosis of PCOS [4]. At the same time, an important remark about ruling out other types of pathology is the most significant.

According to the American Society for Reproductive Medicine (ASRM), the European Society of Human Reproduction and Embryology (ESHRE) (2003), and the International PCOS Network (2018), the presence of any two of the three main criteria enables determination of a certain type (phenotype) of PCOS. The classic phenotype is hyperandrogenism plus polycystic ovary according to US plus anovulation; ovulatory phenotype is represented by hyperandrogenism plus polycystic ovary according to US; non-androgenic type is represented by anovulation plus polycystic ovary according to US; and anovulatory type is represented by hyperandrogenism plus anovulation. The prevalence of these phenotypes and their hormonal and metabolic signs are actively studied in adult women [4–7].

Apparently, it is the categorization of patients under a certain phenotype that underlies the methods of treating PCOS and determines their efficiency.

MATERIALS AND METHODS

The clinical interpretation of the diagnosis of PCOS by specialists among 121 patients admitted to Moscow hospitals for surgical treatment was analyzed, which is the aim of this study.

Initial diagnosis of PCOS was made during outpatient examination. Thus, the study included 121 women of reproductive age with an incoming diagnosis of PCOS and without other factors of infertility (inclusion criteria were an incoming diagnosis of PCOS for hospitalization and the exclusion of tubal-peritoneal and male factors of infertility).

The main complaints of the patients were the absence of pregnancy with regular sexual activity for more than one year without the use of contraception ($n=108$, or 89.2%), menstrual irregularities ($n=60$, or 49.5%), and signs of hyperandrogenism including acne; hirsutism; and dark vellus and/or rod hair on the face, areola, white line of the abdomen (linea alba), and inner thighs ($n=34$, or 28%).

Before ovarian surgery for PCOS, all patients underwent additional examination, including history taking (aspects of menstrual and generative function) and study of anthropometric parameters (body weight and height). Based on these parameters, body mass index (BMI) was calculated, clinical signs of hyperandrogenism (acne, presence of hirsutism, and degree of hirsutism) were assessed, and hormonal profile was determined to detect biochemical hyperandrogenism (free testosterone). In addition, plasma glucose and insulin levels were determined in all patients.

US of the pelvic organs was also performed on all patients ($n=121$), with all results corresponding with the diagnosis of PCOS.

According to the Ministry of Health of the Russian Federation of 2021 [8], the US criteria for PCOS was the presence of 20 or more follicles with a diameter of 2–9 mm in any ovary and/or an increase in the volume of any ovary to 10 cm³ or more when using 8-MHz transvaginal probes (in the absence of a corpus luteum, cysts, or dominant follicles).

Based on the examination results, the patients were diagnosed with PCOS, after which the women were referred to the hospital for surgical treatment.

Gynecological surgical hospitals were conditionally divided into three levels: a city clinical hospital, a research center, and a commercial clinic.

Fifty-four women aged 21 to 37 years (mean age 28.74±3.75 years) were referred to the city clinical hospital (group 1); 48 patients aged 22 to 42 years (mean age 28.81±3.67 years) were referred to a research center (group 2); and 19 women aged 25 to 41 years (mean age 32.89±3.69 years) were referred to a commercial clinic (group 3).

Statistical data processing was performed using the STATISTICA Base software package using parametric and nonparametric methods. Arithmetic means, standard deviations, medians, and percentiles of indicators were calculated.

Confidence limits to the arithmetic mean were calculated based on Student's distribution. The exact 95% confidence limits for frequencies were calculated based on the binomial distribution, and the significance of the difference in frequencies in groups was calculated using the chi-square test.

Due to the fact that some of the studied indicators had distributions that differed significantly from normal, the nonparametric Mann–Whitney and Wilcoxon tests were also used. Differences were considered statistically significant at p lower than 0.05.

The study was approved by the local ethics committee of the I.M. Sechenov First Moscow State Medical University (extract from the LEC protocol dated December 17, 2021, No. 23-21). All patients signed informed consent to participate in the study and publish their medical data.

RESULTS AND DISCUSSION

According to global statistics, PCOS is diagnosed in 6%–20% of women of reproductive age [7], and in the structure of infertile marriages, its frequency ranges from 5% to 22% [8–10]. PCOS has a significant variability of clinical

symptoms and can be manifested not only by hyperandrogenism associated with clinical signs of androgenization and impaired folliculogenesis and menstrual rhythm but also by a wide range of metabolic disorders in the form of obesity, carbohydrate metabolism disorders, and impairment of blood lipid characteristics. Currently, PCOS is considered to be a reproductive metabolic syndrome which is a risk factor for the development of cardiovascular diseases and diabetes mellitus [11, 12]. The prevalence of each isolated symptom that makes up the clinical presentation of PCOS is quite high, but most of the symptoms are nonspecific and can be noted in other diseases or conditions. Therefore, the diagnostic value of a single isolated symptom is doubtful.

Table 1 presents the clinical symptoms manifested by the patients in the study.

According to the clinical recommendations of the Ministry of Health of the Russian Federation (2021), which coincides with the recommendations of ASRM/ESHRE (2003) and the International PCOS Network (2018), the presence of any two of the three main criteria enables determination of a certain type (phenotype) of PCOS. The PCOS phenotype of the patients included in the study ($n = 121$) could not be identified clearly

Table 1. Clinical symptoms in patients included in the study

Symptoms	Number of patients, n (%)	Including by groups		
		group 1 ($n=54$)	group 2 ($n=48$)	group 3 ($n=19$)
Menstrual disorders	60 (49.5)	26 (48)	30 (63)	4 (58)
Infertility:				
primary	81 (66.9)	36 (66.7)	38 (79.2)	7 (36.8)
secondary	27 (22.3)	9 (16.6)	8 (16.6)	10 (52.6)
Total...	108 (89.2)			
History of pregnancies	31 (25.6)	12 (22.2)	9 (18.8)	10 (52.6)
Childbirth in history	18 (14.9)	7 (12.9)	3 (6.3)	8 (42.1)
Abortion	6 (5.0)	3 (5.5)	1 (2)	2 (10.5)
Body mass index (kg/m ²):				
18.5–24.9 (normal)	64 (52.9)	33 (61)	25 (53)	6 (32)
25.0–29.9 (overweight)	29 (23.9)	9 (17)	12 (26)	8 (42)
>30 (obesity)	25 (20.7)	12 (22)	9 (19)	4 (21)
Clinical manifestations of hyperandrogenism	61 (50.4)	21 (39)	29 (60)	11 (58)
Acanthosis nigricans	6 (5.0)	1 (1.9)	5 (10.4)	0
Biochemical manifestations of hyperandrogenism (free testosterone level in pg/ml):				
up to 2.85 (normal)	112 (92.5)	53 (98)	41 (85)	18 (95)
2.85–3.01	3 (2.5)	0	2 (4.2)	1 (5.3)
3.01–3.64	6 (5.0)	1 (1.9)	5 (10.4)	0
Blood glucose above 5.8 mmol/l	11 (9.1)	7 (12.9)	4 (8.3)	0
Insulin level in μ U/ml:				
2.6–24.9	115 (95)	53 (98)	43 (90)	19 (100)
over 25	6 (5.0)	1 (1.9)	5 (10.4)	0
Polycystic ovaries according to ultrasound	121 (100)	54 (100)	48 (100)	19 (100)

based on the results. Considering that US was performed on all patients examined for surgery, it was possible to consider them as a classic variant of the pathology represented by hyperandrogenism, polycystic ovaries according to US data, and anovulation.

A thorough analysis of all parameters that determined the clinical symptoms and the initial diagnosis of PCOS was performed. First was menstrual irregularities, which were reported by 49.5% of the patients. The criterion for diagnosing an irregular menstrual cycle in women of reproductive age was a cycle duration of >35 days or <8 menstrual cycles per year [13, 14].

The durations of the menstrual cycles of the patients is presented in Table 2.

In group 3, patients with a menstrual cycle duration of 26–35 days were statistically significantly more common (15 cases or 78.9% versus 51.8% in group 1 [$p=0.0137$] and 37.5% in group 2 [$p=0.0006$]).

In group 3, patients with a menstrual cycle duration of 36–90 days were statistically significantly less common (2 patients or 10.5% versus 33.3% in group 1 [$p=0.0114$] and 50% in group 2 [$p=0.0001$]).

There were no statistically significant differences between groups in the number of patients with a menstrual cycle longer than 90 days.

It is noteworthy that menstrual irregularities are not a mandatory criterion for the diagnosis of PCOS. Anovulatory cycles are possible even with regular menstrual bleeding. In case of menstrual irregularities, the diagnosis of PCOS should be specified by other criteria.

According to the results of the preliminary selection of patients with PCOS for surgical treatment, 108 (89.2%) of them had primary or secondary infertility.

These complaints were analyzed depending on the group of women (hospital level). Primary infertility was registered in

36 (66.7%) women in group 1, in 38 (79.2%) cases in group 2, and in 7 (36.8%) cases in group 3. Secondary infertility was revealed in 9 (16.6%) female patients in group 1, in 8 (16.6%) cases in group 2, and in 10 (52.6%) patients in group 3.

Summarized data on the duration of infertility are presented in Table 3.

When comparing the groups according to infertility parameter, it was revealed that in group 1, statistically significantly less than those in group 2, the patients had a duration of infertility from 1 to 3 years (19 people, or 35% of the group [$p=0.005$]). Patients with infertility duration from 4 to 10 years in group 3 were statistically significantly less common (2 people, or 10%) than those in group 2 (16 people, or 33% [$p=0.013$]) and those in group 1 (22 people, or 41% [$p=0.001$]). Patients with infertility lasting more than 10 years in group 3 (5 people, or 26%) were statistically significantly more common than those in group 2 (1 patient, or 2% [$p=0.0167$]) and in group 1 (4 patients, or 7% [$p=0.0494$]).

At the same time, the frequency of primary infertility prevailed over the indicators of secondary infertility in women with an initial diagnosis of PCOS. Eighty-one (66.9%) patients had primary infertility, and 27 (22.3%) patients had secondary infertility.

When analyzing the generative function of patients with an initial diagnosis of PCOS, the following results were obtained: A history of pregnancy was noted in 12 (22.2%) female patients in group 1, in 9 (18.8%) women in group 2, and in 10 (52.6%) cases in group 3. Pregnancy outcomes in patients in group 1 were childbirth in 7 (12.9%) women, spontaneous miscarriage in 3 (5.5%) cases, and abortion in 3 (5.5%) cases. One woman from group 1 had a history of one birth and one abortion.

In group 2, pregnancy outcomes were 3 (6.3%) deliveries, 1 (2%) abortion, 3 (6.3%) spontaneous miscarriages, and 1 (2%) ectopic pregnancy.

Table 2. Duration of the menstrual cycle in the examined patients

Patient group	Number of patients with a given menstrual cycle duration		
	26–35 days	36–90 days	more than 90 days
Group 1	28	18	8
Group 2	18	24	6
Group 3	15*	2*	2

* $p < 0.05$.

Table 3. Duration of infertility in the examined patients with an initial diagnosis of polycystic ovary syndrome

Patient group	Duration of infertility (years)		
	1–3	4–10	more than 10
Group 1	19*	22	4
Group 2	29	16	1
Group 3	10	2*	5*

* $p < 0.05$.

In group 3, pregnancy outcomes were 8 (42.1%) deliveries, 2 (10.5%) abortions, and 1 (5.2%) spontaneous miscarriage.

It should be noted that a history of pregnancy and childbirth should not confirm the diagnosis of PCOS. In case of indications of their presence in the history, a more thorough examination of patients is required, and the diagnosis of PCOS should be clarified according to other criteria.

According to current data, PCOS patients more often have abdominal-type obesity ("apple"). PCOS coexisting with obesity leads to the development of insulin resistance. Obesity in PCOS is a risk factor for the development of cardiovascular diseases, endometrial cancer, and decreased generative function [15]. Thus, BMI should be determined in all patients with suspected PCOS [16]. This parameter was analyzed in the examined patients.

There were no statistically significant differences in BMI between the groups.

The average BMI in group 1 was 25.34 ± 3.72 kg/m² (body weight deficit in 2%, normal body weight in 61%, overweight in 17%, degree I obesity in 15%, and degree II obesity in 5%). The average BMI in group 2 was 26.11 ± 4.5 kg/m² (body weight deficit in 2%, normal body weight in 53%, overweight in 26%, degree I obesity in 15%, and degree II obesity in 4%). The average BMI in group 3 was 27.12 ± 3.89 kg/m² (body weight deficit in 5%, normal body weight in 32%, overweight in 42%, degree I obesity in 10%, and degree II obesity in 11%).

Thus, among the patients examined, 64 (52.9%) had BMI within the reference values, 29 (23.9%) were overweight, and 25 (20.6%) were obese. Considering that being overweight and obesity are frequent components of PCOS, the question of making this diagnosis in 64 (52.9%) patients with normal height/normal body weight raises some doubts.

The prevalence of hirsutism in the classic PCOS phenotype reaches 75% [5].

According to the clinical recommendations of the Ministry of Health of the Russian Federation for PCOS (2021), certain assessment methods should be applied in the presence of clinical hyperandrogenism (acne, hirsutism, and scalp hair loss). It is recommended that, for women with complaints hirsutism, hirsutism score be calculated to assess the severity of hirsutism according to the modified Ferriman–Gallwey scale [5].

It is important to bear in mind that the severity of hirsutism in PCOS does not always correlate with the degree of androgen excess. Severe hirsutism can occur with a slight increase in serum androgen levels, and a significant increase in levels is not always accompanied by hirsutism. This discrepancy between the level of hormones and the severity of hirsutism indicates the different individual sensitivity of the target tissue to these hormones [17].

Among the study participants ($n=121$), 50 (41.3%) women noted clinical signs of hyperandrogenism in the form of dark hair on the face, areola, linea alba, and inner thighs; 11 (9%) patients complained of acne of varying severities

(on the face, upper chest, upper back, and shoulders); and 18 (14.8%) women had a combination of several signs.

In group 1, 18 (33.3%) women noted the growth of dark hair on the face, areola, linea alba, and inner thighs; 3 (5.5%) patients complained of acne of varying severities (on the face, upper chest, upper back, and shoulders); and 7 (13%) women had a combination of several symptoms.

In group 2, 23 (48%) patients noted the growth of dark hair on the face, areola, linea alba, and inner thighs; 6 (12.5%) women complained of acne of varying severities (on the face, upper chest, upper back, and shoulders); and 8 (16.6%) patients experienced a combination of several signs.

In group 3, 9 (47.3%) patients noted the growth of dark hair on the face, areola, linea alba, and inner thighs; 2 (10.5%) women complained of acne of varying severities (on the face, upper chest, upper back, and shoulders); and 3 (15.8%) patients had a combination of several symptoms.

Thus, clinical manifestations of hyperandrogenism were seen in 61 (50.4%) patients. Therefore, the reasonability of the diagnosis of PCOS in 49.6% of women is questioned.

As one of the markers of PCOS, the level of free testosterone in the blood should be measured in all women with suspected PCOS by the calculation method, using the free androgen index or bioavailable testosterone to assess the presence of biochemical hyperandrogenism [5].

The examination results of the study participants with an initial diagnosis of PCOS were analyzed.

It was found that levels of free testosterone above the reference value (>2.85 pg/ml) were seen in only 9 (7.4%) out of 121 patients. In 112 women, this parameter was within the upper limit of the reference values (mean value 2.78 ± 0.36 pg/ml) and was associated with clinical manifestations of hyperandrogenism. In 9 (7.4%) women, the level of free testosterone was within the range of 2.85–3.64 pg/ml, and in only 6 (5.0%) women, it exceeded the reference values significantly (3.01 to 3.64 pg/ml).

Along with the clinical manifestations of hyperandrogenism in the form of hirsutism, another dermatological manifestation of PCOS, acanthosis nigricans, was noted in these 6 (5.0%) patients with free testosterone levels ranging from 3.01 to 3.64 pg/ml. Acanthosis nigricans (papillary pigmented degeneration of the skin in the form of localized areas of brown hyperpigmentation in skin folds, more often on the neck, armpits, and inguinal region and histologically characterized by hyperkeratosis and papillomatosis) often accompanies PCOS and is one of the clinical markers of insulin resistance in PCOS patients [5].

The initial examination of each PCOS patient should include an assessment of glycemic status; for this purpose, fasting blood glucose levels, an oral glucose tolerance test, or a study of the level of glycated hemoglobin in the blood are used [18].

An increase in blood glucose levels above 5.8 mmol/l was detected in 11 (9.1%) patients in the study. An increase

in blood glucose levels was associated with obesity in 3 (5.5%) patients in group 1 and in 1 (2.1%) patient in group 2. Correlation with being overweight was noted in 2 (4%) patients in group 1 and in 3 (6.3%) cases in group 2.

The Ministry of Health of the Russian Federation on PCOS (2021) does not recommend insulin levels as a mandatory parameter for diagnosing or verifying PCOS [5, 19]. Nevertheless, the results of the study of this parameter in the research participants were analyzed.

Insulin has an extremely wide range of normal values, from 2.6 to 24.9 $\mu\text{U/ml}$. Taking values exceeding 25.0 $\mu\text{U/ml}$ as a reliable boundary of laboratory hyperinsulinemia was possible. The results revealed that 115 (95.1%) patients had normal values for this parameter and only 6 (5.0%) cases had results that significantly exceeded the upper limit of normal (Table 1).

It is noteworthy that these six patients had acanthosis nigricans together with clinical and biochemical manifestations of hyperandrogenism as well as obesity. The presence of this symptom complex with a high degree of probability enables categorizing these patients as having classic manifestations of PCOS.

Since 2003, clinical guidelines for PCOS have included the determination of the morphological structure of the ovaries using US as an independent and isolated diagnostic criterion. Pelvic US is recommended for all patients with suspected PCOS to verify the diagnosis [5]. Ultrasonographic criteria for polycystic ovaries include the following:

- when using 8-MHz transvaginal sensors, the presence of 20 follicles or more with a diameter of 2–9 mm in any ovary and/or an increase in the volume of any ovary up to 10 cm^3 or more (in the absence of a corpus luteum, cysts, or dominant follicles) and
- when using transvaginal sensors with lower resolution characteristics or during transabdominal examination,

an increase in the volume of any ovary up to 10 cm^3 or more (in the absence of a corpus luteum, cysts, or dominant follicles) [5, 19, 20].

In all patients included in the study, echographic signs of PCOS were revealed. PCOS was confirmed through US in 54 women in group 1, in 48 women in group 2, and in 19 women in group 3.

Thus, US study results became fundamental for the diagnosis of PCOS and were the leading criterion. In all patients included in the study and referred for surgical treatment, US signs of pathology were associated with obesity, clinical and/or biochemical hyperandrogenism, or menstrual and generative dysfunction. In only six patients, a diagnosis of PCOS according to the majority of pathognomonic signs was established.

CONCLUSION

The results suggest an unreasonably broad interpretation of the diagnosis of PCOS. In this regard, it must be borne in mind that the diagnosis of PCOS is, to a certain extent, a diagnosis of exclusion. Only a multiple, extended, thorough, and comprehensive examination of patients with a suspected diagnosis of PCOS will allow better understanding of their individual characteristics and offer adequate methods for correcting the symptom complex in order to improve overall health, fertility, and quality of life.

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