Polycystic ovary syndrome – controversy in the diagnosis

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Abstract

Polycystic ovary syndrome (PCOS) is found in 3 to 6% of women in child-bearing age. At the same time PCOS is the most common cause of infertility. The diagnostic criteria for PCOS include: anovulation or ovulatory disorders, hyperandrogenism and typical polycystic ovary image in ultrasound examination in the absence of other causes of hyperandrogenism. The etiology of the syndrome remains unknown, nevertheless it seems that abnormal regulation of cytochrome P450-17alfa may be the underlying cause. Impaired regulation of abnormal androgen metabolism is closely related to increased level of luteinizing hormone (LH) and hyperinsulinemia. The most common clinical symptoms include: menstrual disorders, hirsutism and acne. Obesity is found in 30 to 60% of PCOS patients. Increased body weight in PCOS patients is often accompanied by more intense clinical symptoms than in not obese PCOS patients with similar biochemical disorders observed. Today the majority of clinical practitioners in the world recognize the Rotterdam criteria published in 2003, nevertheless the recommendations of National Institute of Health in the USA from 1990 are also commonly followed. In 2009 Androgen Excess and PCOS Society published reviewed recommendations for PCOS diagnosis. Despite the fact that there are three different diagnostic recommendations published the interpretation of three basic groups of PCOS symptoms is in many ways controversial. The assessment of hyperandrogenisation is largely subjective and may be done by means of various scoring systems. The measurement of androgen concentration is an issue due to the absence of easily accessible and at the same time precise laboratory methods. Similarly, the assessment of ovulation is not standardized. Evaluating the structure of the ovary in the ultrasound examination is problematic as the methods suggested in the Rotterdam criteria are time-consuming and difficult to apply. As a result different physicians may diagnose PCOS in women with various phenotypes.

Key words: hirsutism, polycystic ovary syndrome (PCOS)

Introduction

It was already in 1935 that Stein and Leventhal described the following coexisting symptoms in seven women: hirsutism, obesity, menstrual disorders and bilaterally enlarged cystic ovaries. Their report provided the basis for clinical definitions of PCOS [1]. Since then our understanding of PCOS has evolved so dramatically that none of the originally described features of the syndrome is now treated as obligatory in diagnosing PCOS, including the presence of polycystic gonads which is exactly the symptom from which the name of the syndrome was derived.

Currently physicians all over the world have three official clinical definitions of PCOS at their disposal: the definition of the National Institute of Child Health and Human Development – NICHD dated 1990 summarized and published two years after it was established; the one by the European Society of Human Reproduction and Embryology/American Society of Reproduction Medicine (ESHRE/ASRM criteria published in 2003 in Rotterdam [2]) and the newest criteria developed by Androgen Excess and PCOS Society under the leadership of Ricardo Azziz (AEPCOS dated 2009) [3]. In fact, all definitions encompass similar criteria, however there are small differences that imply significant changes in diagnosing PCOS in women with various phenotypes. The definitions mentioned above are presented and compared in Table 1.

The fact that there are many coexisting definitions of PCOS makes it difficult to determine the frequency of the syndrome. Nevertheless convincing data have been elaborated indicating that PCOS is found in 6 to 8% of women in the general population [4]. Moreover, it is known that the syndrome is the most common endocrine disorder found in women in child-bearing age, therefore it is a major problem in the public health domain [5].

In the study we would like to discuss the problems related to PCOS diagnosis basing on current diagnostic criteria especially in the realm of clinical and laboratory...
research. In the study we will characterize main stand-
points held by specialists in gynecological endocrinology
and present some indications useful in clinical practice.

Table 1. Comparison of existing statements
regarding the diagnosis of PCOS

<table>
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<th>Society</th>
<th>Criteria</th>
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| National Institute of Child Health and Human Development – NICHD (1990) | both:
  - clinical and (or) biochemical symptoms of hyperandrogenism;
  - oligo- or anovulation                                               |
| European Society of Human Reproduction and Embryology/
  American Society of Reproduction Medicine (ESHRE/ASRM or Rotterdam) (2003) | two out of three criteria present:
  - clinical and (or) biochemical symptoms of hyperandrogenism;
  - oligo- or anovulation;
  - polycystic ovaries (noted in USG examination)                     |
| Androgen Excess and PCOS Society (AEPCOS) (2009)                        | both:
  - hyperandrogenism: hirsutism and (or) hyperandrogenemia;
  - ovarian dysfunction: oligo- or anovulation and (or) polycystic ovaries |

* Elimination of other known causes of hyperandrogenisation is required in each case to diagnose the syndrome

We hope that such approach to the subject will be a good
incentive to determine better and more precise diag-
nostic tools for PCOS diagnosis. Due to constraints as to
the length of the study we focused only on the contro-
versy surrounding diagnosing in relation to three groups
of symptoms (ovulatory disorders, hyperandrogenisation
and hyperandrogenemia as well as the evaluation of the
ovaries in the ultrasound examination). We consciously
omitted the discussion of many doubts related to addi-
tional clinical features of the syndrome (for example
metabolic disorders), treatment or exclusion of other

disorders.

Ambiguity in the evaluation of menstrual and ovula-
tion disorders

According to diagnostic criteria for PCOS applied by
ESHRE/ASRM one of the characteristic features of the
syndrome is oligo- and (or) anovulation. Still, these so-
cieties fail to explain the terms in detail both in their
descriptive and methodological aspects [6]. It is under-
standable that in women with menstrual disorders
ovulation is affected as well – in fact irregular menstrual
bleeding is the consequence of that. Nevertheless cur-
rent guidelines do not address the question of time on
the basis of which oligo- or anovulation is diagnosed.

Most often oligomenorrhea is assumed to mean
menstrual bleeding occurring every 35 or more days or
less than 10 bleedings a year. The problem of diagnosing
the secondary amenorrhea is more complicated. It has
been quite commonly acknowledged that the absence of
menstrual bleeding lasting more than 3 months allows to
diagnose secondary amenorrhea, however many authors
and clinical practitioners diagnose it after six or more
months with no menstrual bleeding [7]. The discrepancy
is particularly visible when comparing American and
European authors and it gives rise to differences in the
clinical description of PCOS patients even if the descrip-
tion is based on the same clinical definition of the syn-
drome.

Both oligo- and amenorrhea thereof are the symp-
toms of ovulation disorders that are clinically apparent.
It is estimated that this affects approximately 75-85% of
patients diagnosed with PCOS [8]. On the other hand,
the frequency of the syndrome in patients with men-
strual disorders is estimated to be 15-23% [9]. Additio-
nally, ovulatory disorders are also manifested in PCOS
patients as frequent menstrual bleedings (polymenor-
rhrea – bleeding more often than every 26 days) found
relatively rarely in these patients – in approximately
1-2% [9]. Even when we consider all types of menstrual
disorders it is estimated that none of them is found in
approximately 30% of PCOS patients (eumenorrhea),
which does not mean that this group of patients ovulate.

Non-apparent clinical ovulation disorders

Chang et al. [9] stated that in 16% of 316 PCOS pa-
tients who had not undergone treatment menstrual
bleeding was regular, every 27-34 days, which did not
mean however that the cycles were ovulatory. In the
studies involving more patients the percentage of wo-
en with normal menstrual cycle ranged between 15
and 40%. The percentage was bigger in the studies con-
ducted according to the Rotterdam criteria and smaller
in those that followed the older NICHD statements [10].

In practice it is important to detect coexisting ovula-
tory disorders in patients diagnosed with eumenorrhea.
Currently it is believed that the following two methods
are the most useful. The first one is a repeated ultra-
sound examination of the ovaries that allows to deter-
mine the presence of ovarian follicle which is then trans-
formed into corpus luteum. The ultrasound visualiza-
tions showing the absence or rapid decrease of the
dominant follicle seem to be the most sensitive and the
most specific methods to evaluate ovulation (84 and
89.2% respectively). At the same time, it is very useful
to specify other parameters, especially the presence of free fluid in cul-de-sac as well as irregular shape of the follicle [11]. Another widely applied method to evaluate ovulation is the measurement of progesterone concentration in the luteal phase (i.e. 20-24 day of the cycle) [12]. Progesterone concentration lower than 3-4 ng/ml (measurement dependent on the method) indicates that the cycle was anovulatory. These widely recognized criteria have their limitations. Therefore, one needs to remember that the suggested norms should be treated with caution. Inadequate moment for progesterone measurement may for obvious reasons leading to improper diagnosis of the ovulatory disorder. Measuring the concentration of progesterone as a method of evaluating ovulation may be useful in many situations if there is no need to repeat the measurement many times. On the other hand, the method is retrospective and as such it shows the ovulation that has already ended which has no advantage for women who are trying to get pregnant [10].

Another contentious issue related to the evaluation of normal ovulation is the importance of a single observation of anovulatory cycle in a patient with eumenorrhea. The experience gained so far shows that anovulatory menstrual cycles are rare in healthy women, therefore even a single observation of such a condition has a great predictive value. Still, it is believed that if the first cycle being monitored was anovulatory the next one should be observed and we may identify ovulatory disorder only when anovulation is observed again [13].

Ovarian morphology

The first description of a PCOS case was published by Stein and Leventhal in 1935 [1]. Another feature considered by them as a basic characteristics of the syndrome apart from abnormal ovulation is abnormal polycystic ovarian morphology. Currently, PCOS is seen mostly as a functional disorder, therefore identification of polycystic ovaries is not required to make the diagnosis. On the contrary, the mere presence of such gonadal morphology is not sufficient to make the diagnosis [14].

There are three morphological features determining the identification of polycystic ovary morphology including the number and size of follicles, ovarian volume and ovarian stroma volume. The Rotterdam criteria address only two parameters. This definition assumes that a polycystic ovary in three planes contains 12 or more follicles of 2 to 9 mm in diameter (contrary to earlier definitions which took into account the number of follicles in a single biggest cross section of the ovary) and (or) has a volume of over 10 ml [15].

The Rotterdam criteria emphasized that detailed measurements of the ovary and the follicles may not be replaced with generalized and subjective impression of a physician. Moreover such features of an USG image as peripheral location of the follicles, echogenicity or the area of ovarian stroma should not be taken into consideration. The criteria also specify how to count ovarian follicles. Three dimensions of an ovary should be taken into account: transverse, longitudinal and anteroposterior. The size of a follicle should be calculated in a similar way with its three dimensions taken into account.

The diagnostic criteria for USG examination according to ESHRE/ASRM consensus are thus very precise, however in practice they are very difficult to apply. Counting and measuring the follicles in three planes is very complicated and time-consuming, especially when two-dimensional USG technique is used. Three-dimensional (3D) technique may be useful as its accuracy is estimated to be over 95% [16]. On the other hand the data on the use of 3D USG are still limited for PCOS, similarly to the accessibility of the technique (transvaginal 3D ultrasound) especially in middle-income developing countries.

Making reference to the Rotterdam criteria it is worth to emphasize that the cut-off point for 12 follicles has been adopted for PCOS based on the data derived from one study only. The authors of this publication found 99% specificity and 75% sensitivity when comparing polycystic ovary syndrome with a control group. It should be kept in mind that only 214 women suffering from the syndrome had been included in the study which seems to be a very small number considering the absolute number of women with PCOS (the population of PCOS patients in the USA estimated to be 12-37 million) [17]. To analyze the diagnostic values of related variables the authors of this study took into account only three follicle size ranges (2-5, 6-9 and 2-9 mm) and six cut-off points for the number of follicles (3-5, 10, 12, 15). The conclusions of the study referring to the norms were not confirmed in subsequent studies. For example, in the study by Diamanti-Kandarakis et al. [5] 58% of patients in the control group had more than 12 follicles in an ovary.

The second ultrasound examination criterion specified in the Rotterdam criteria is also a controversial one. The volume exceeding 10 cm³ as a diagnostic feature for PCOS has been determined on the basis of several publications where increased ovarian volume was found in women diagnosed with PCOS. However, in some of the newest studies it has been observed that the
volume of normal ovaries does not exceed 7.7-7.5 cm³, therefore these values should be considered as abnormal. Azziz confirmed these findings. In their study the cut-off point set for 10 cm³ ensured sensitivity and specificity: 98.2 and 45%, whereas 7 cm³: 91.2 and 67.5% [3].

To sum up the statements regarding the criteria for ultrasound examination that are currently followed in case of PCOS, it should be emphasized that proper practical application thereof is very difficult and based on uncertain evidence. Amer et al. [4] found that the consensus between the researchers in the studies where ultrasound examination was used amounted only to 51%. Another finding made in the same study was that the diagnosis made by the same researcher at different times was identical only in 69% of cases. Considering all these reservations it should be noted that many physicians apply their own criteria based both on numerical data (increased volume of the gonad, greater number of follicles and greater diameter thereof) and on “general impression” (peripheral distribution of follicles, increased echogenicity of the ovarian stroma or enlarged area or volume thereof). There are also many studies examining the importance of more modern ultrasound techniques such as a 3D ultrasound examination, a Doppler ultrasound and the combination of these tests.

Undoubtedly, if ovarian ultrasound is to remain a diagnostic criterion for PCOS new and more reliable standards for interpretation of the results of this test are needed.

**Hyperandrogenisation controversy**

Hyperandrogenisation understood as a group of clinical symptoms related to increased concentration of active androgens in circulation in women is one of three main diagnostic criteria for PCOS. The classic symptoms of hyperandrogenisation include excessive, abnormal hair (hirsutism), androgenic hair loss and acne. In its severe form hyperandrogenisation manifests as virilisation (virilism). The syndrome is characterized by enlargement of the clitoris (clitoromegaly), deepening of voice and development of masculine body structure. In practice, PCOS patients rarely present with the condition, which is characteristic rather for androgen-secreting tumors [18]. The clinical evaluation of hyperandroge

nism is an intricate issue especially as far as the achievement of maximum objectivity of the examination is concerned. Despite the fact that there are many detailed clinical descriptions of PCOS, in modern medicine great importance is attached to different types of scales which to some extent ensure impartiality of the evaluation made by a given physician. Apart from such impartiality point scales used to assess the intensity of symptoms have also other advantages. They allow to compare the intensity of the symptoms and choose adequate treatment and they work well in scientific research. Still, sufficient reliability and acceptance by a wide circle of clinical practitioners are essential prerequisites for such scoring systems to be applied [11]. In case of PCOS it is common to apply the scales that refer to the severity of hyperandrogenism, especially in case of hirsutism but acne and hair loss as well. Nevertheless, the selection and application of a given scale are controversial.

**Hyperandrogenemia**

It is estimated that 60 to 80% of patients diagnosed with PCOS present with increased concentrations of androgens circulating in the blood. It should be emphasized however that many issues related to hyperandrogenemia in women diagnosed with PCOS remain debatable as the following questions have still not been resolved in a definite way: which androgens should be tested, what is the exact moment when androgen concentration should be tested, how to interpret the results and, above all, which analytical techniques should be used [19]. The last problem is currently the most important in the discussion over the appropriate evaluation of hyperandrogenemia in PCOS patients. Similarly to other hormones found in the circulation in the form bound to proteins, only the non-bound (free) hormones are biologically active. Therefore, the major indication of hyperandrogenemia is free testosterone (fT). Moreover, it is known that its concentration is often increased in women suffering from PCOS. As a result, the measurement of fT in the blood is considered as the most sensitive biochemical marker in PCOS diagnosis [20]. One of two methods may be used to measure the concentration of fT: either a direct laboratory test or a calculation of the index on the basis of total testosterone level and sex hormone binding globulin (SHBG) level. Total testosterone measured in the blood includes the pool bound to SHBG, thus additional measurement is needed. It should be kept in mind that in patients diagnosed with PCOS decreased levels of SHBG are observed as a result of interference between hyperinsulinemia and hepatic synthesis of this globulin [43]. A single measurement of SHBG and fT levels with the use of a proper measurement method in case of this disorder has a great diagnostic value. Moreover, the level of SHBG is a good marker of insulin resistance, therefore the measurement is useful also to diagnose metabolic disorders observed in the syndrome discussed [16].
Among methods available to determine the level of fT there is the radio immunological method (RIA), the equilibrium dialysis and chromatographic methods.

The RIA method is commonly available, but it yields accurate results only when the concentration of free testosterone is relatively high (for example in men). In women the RIA method fails to properly reflect the levels of testosterone: both free and bound [7]. In practice, the immunological method that has proven to be the best is the direct double RIA of high quality. Still, it is proposed that the variability index between individual tests be lower than 10% of the normal range specified by the laboratory where the tests are conducted. The normal range for the test should be determined locally in scrupulously chosen female population not presenting an increased level of androgens.

The direct methods to determine the serum level of fT such as equilibrium dialysis are very exact and their results are in correlation with the results of mass spectrometry. Still, they are not commonly available, mainly due to technical difficulties and high costs.

The importance of measuring androgens other than testosterone, such as androstenedione, dehydroepiandrosterone (DHEA) and dehydroepiandrosterone-sulfate (DHEAS), is a point of dispute in PCOS diagnosis. It needs to be noted that currently there is no scientific evidence available to show clinical validity of androstenedione level determination. It is estimated that approximately 10% of PCOS patients present with increased level of this androgen, but it is unknown how such increased level correlates with clinical manifestation of the syndrome [18].

It should be emphasized that DHEA measurements are not useful in clinical practice. The hormone is found in the circulation in very low concentration and its release exhibits a pulsatile pattern. It is even more complicated to interpret the result of DHEA test due to the fact that its concentration is largely dependent on the patient’s emotional condition as stress (e.g. associated with being admitted to hospital) may cause a significant rise in the release of the hormone. Adrenal DHEA metabolite – DHEAS is a much better marker for hyperandrogenemia in PCOS. Its secretion is relatively stable both in daily and monthly patterns and its concentration is sufficiently high to reliably determine the exact value. DHEAS is an adrenal marker of hyperandrogenemia as it is secreted mostly (over 95%) by the adrenal glands. In PCOS increased level of DHEAS is found in approximately 25-35% of patients and despite the fact that this androgen is not a marker of ovarian dysfunction, determination of increased concentration thereof is sufficient to diagnose hyperandrogenemia [19].

**Hirsutism**

Hirsutism is a condition of excessive male-pattern hair growth in women resulting from increased androgen production and/or increased skin sensitivity to androgens. As a symptom of hyperandrogenisation, hirsutism appears usually together with other symptoms of masculinization such as: acne, androgenic hair loss, seborrhea, enlargement of clitoris, deepening of voice and defeminization including anovulation, menstrual disorders and nipple retention. Increased secretion of androgens, which is usually the underlying cause of hirsutism, leads also to metabolic changes such as hyper-insulinism, insulin resistance, obesity, changes in lipid profile. The frequency of hirsutism symptoms varies depending on the geographic region. In Central Europe such changes of various intensity are found in approximately 30% of women [19]. In Poland, according to different authors, the problem affects 3 to 10% of women in the general population [1]. Asian women usually have less body hair than females from the Mediterranean region. The frequency of the symptom varies also with age: hair on the upper lip is found in approximately 1/3 of women after menopause [19].

Physical appearance plays an important role, especially for women. Women try to conform their physical appearance to the common standards, however current female beauty canons are very far away from the realistic appearance of most of the people. Skin conditions in the form of hirsutism, acne or hair loss (baldness) resulting from a disease may significantly interfere with psychological and social life of the patients.

The symptom is defined as excessive growth of terminal (thick) hair in women in locations on the body and on the face that are typical for men. The condition affects approx. 5-15% of women, depending on the adopted definition of PCOS [1, 19]. Excessive and abnormal hair growth (i.e. on those parts of the body where normally terminal hair is not found) is the most common clinical manifestation of hyperandrogenism. It is estimated that approx. 80-90% of women suffering from pathologically elevated level of androgens present with hirsutism. In case of PCOS it is estimated that the frequency of the condition is as high as 70%. Despite the fact that some of the clinical practitioners consider hirsutism mainly in terms of a cosmetic problem, it is one of the most crucial factors deteriorating the quality of life in women suffering from PCOS [11, 16].
Clinical evaluation of the symptom’s aggravation depends largely on individual impression of a given physician. The medical personnel should also take into account that the patient may perceive the problem in a different way. According to Espinos [12] even in case of patients who follow the same evaluation scale as the medical personnel (Ferriman and Gallwey score) self-assessment in terms of hirsutism largely diverges from the physician’s opinion. In the same study it has been proven that only the assessment made by a professional with the use of Ferriman-Gallwey score correlates in a significant manner with the severity of hyperandrogenemia [13].

It is worth to remember that the age and the ethnic background have a considerable impact on the pattern and the intensity of hair growth mainly due to inherited factors (e.g. genetic differences in the activity of 5α-reductase). As far as Asian women are concerned we may expect to observe less intense terminal hair growth in comparison to women representing other ethnic groups (e.g. women of Mediterranean or Indian origin) [6].

As already mentioned, one of the biggest difficulties in the evaluation of hirsutism is the assurance of maximum objectivity of the examination. Currently the main tool used to ensure objectivity of the examination is the application of Ferriman-Gallwey score in everyday practice. The scale proposed in 1961 is used to assess the severity of hair growth from 0 to 4 (where 0 means a lack of terminal hair and 4 means hair growth of adult male pattern). Terminal hair may be differentiated from original hair mainly by its length (over 0.5 cm), coarseness and pigmentation. The original Ferriman-Gallwey score took account of eleven anatomical regions and the sum of points given in the evaluation of these regions was decisive in determining the severity of hirsutism. The commonly accepted cut-off level for defining the condition is a sum equal or bigger than 8, nevertheless the issue remains controversial. Some of the authors propose to take the sum equal to 3 or 5 as the cut-off point. Many physicians developed various modifications of the score. The modifications concern mostly the kind and number of body regions included in the scale. It was Ferriman himself who proposed the most significant change. He figured out that the intensity of hair growth in the region of forearms and shins does not correlate with hair growth in the remaining nine body regions under evaluation (so called hormonal hair). Therefore, these two body regions of the human body have been excluded from the evaluation [15]. Such modified form of Ferriman-Gallwey score after some years became the most widespread scoring system both in clinical and in scientific studies.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Scale</th>
</tr>
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<tbody>
<tr>
<td>Oanforth and Tratter</td>
<td>1922</td>
<td>hair color: fair, medium, dark; 0: no body hair except pubic and underarm hair; 1: terminal hair in any other body region than pubic and underarm areas</td>
</tr>
<tr>
<td>Beek</td>
<td>1950</td>
<td>amount of terminal hair (0.5 cm) in several locations – on the head, trunk, arms, legs, in pubic and underarm area</td>
</tr>
<tr>
<td>Shah</td>
<td>1957</td>
<td>terminal hair (0.5 cm); total value = quality × thickness × fraction of the body region; nine body regions: face, stomach, chest, arms, forearms, thighs, legs, bottom and upper back</td>
</tr>
<tr>
<td>Lunde and Grottum</td>
<td>1984</td>
<td>terminal hair (0.5 cm); four grades (0-3); 19 body regions: eyebrows, lips, chin, cheeks, upper back, arms, forearms, hands, nipples, breasts, sternum, upper stomach, lower stomach, genital area, lower back, thighs, legs, scalp; the total value of 16 or above defines hirsutism</td>
</tr>
<tr>
<td>American Society for Reproductive Medicine</td>
<td>2006</td>
<td>modified Ferriman-Gallwey score; 12 body regions: upper lip, cheeks, chin, jaw, upper back, lower back, arms, thighs, chest, upper stomach, linea alba, crotch</td>
</tr>
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</table>

It is worth to emphasize that many other scales of hirsutism evaluation have been proposed. The most important ones, including the one developed in 2006 by AES, have been summarized in Table 2.

**Acne**

Acne is yet another, apart from hirsutism, crucial cosmetic problem affecting PCOS patients. Androgens are capable of stimulating the production of sebum in sebaceous glands, which in turn results in optimal conditions for colonization of bacteria such as Propionibacterium acnes [11].

Despite the fact that acne is considered as crucial symptom of the syndrome, there is a lot of controversy related to the frequency and severity of this dermatose in PCOS patients. The estimated frequency in women suffering from PCOS has a very wide range – from ap-
proximately 20 to 40% [5, 14]. The exact number remains unknown as no large population-based studies have been conducted. Moreover, most of the studies are based on PCOS definition that is different from the currently adopted one, therefore it covers different groups of patients.

The assessment of acne severity in PCOS is yet another problem. Scoring systems (photographic methods, the Leeds technique, lesion counting) are reliable and they are used in dermatology in order to facilitate the decision making process as to the therapy and the evaluation of the reaction to treatment [10]. Such scoring systems however are rarely used by gynecologists, thus our knowledge about the exacerbation of acne in PCOS patients is limited. Similarly, there is no evidence to show a clear correlation between hyperandrogenemia and aggravation of skin lesions. It should be emphasized that there is no definite evidence to prove whether the actual frequency of acne is greater in women suffering from PCOS in comparison to the general population [11].

Hair loss

For the majority of physicians it is obvious that male-pattern hair loss (i.e. hair becoming thinner on the top of the head with a patch of hair left at the front) is associated with hyperandrogenemia. This thesis is strongly supported by historical evidence as baldness in women suffering from PCOS in the past was considered as a typical feature of the syndrome. Nevertheless, modern studies dealing with hair loss in PCOS patients yield very incoherent results. The frequency of the condition ranges from 5 to 50% in various publications which casts doubt on the statement that hair loss is more frequent (or more severe) in PCOS patients [4]. The application of different assessment methods is a crucial cause of such discrepancies in hair loss evaluation. It should be also stated that the objective methods developed to assess the severity and aggravation of hair loss are rarely used by gynecologists.

Hair loss as the only symptom of PCOS is extremely rare. In one of the studies involving women with hyperandrogenisation manifested exclusively with hair loss, only 10% of participants were diagnosed with PCOS [18].

To sum up the presented data on the frequency of hair loss in PCOS and – the other way round – the frequency of PCOS in women suffering from hair loss, it should be noted that this symptom presents little sensitivity and specificity in detecting hyperandrogenemia in case of this syndrome. On the other hand, it has been well documented that hair loss is a more frequent condition in women with excessive androgens. It is also well known that there is no clear relationship between aggravation of hyperandrogenemia and hair loss. This may be easily understood because we are aware that dihydrotestosterone (DHT) is the most significant hormonal stimulus for a hair follicle. Its synthesis takes place to a large extent in skin tags and its effect on the skin is mainly paracrine [18].

In the evaluation of the condition of women affected by hair loss one needs to take into account also other causes of this condition except for hyperandrogenemia, in particular environmental factors (pollution, irritation caused by hair care cosmetics), inherited factors (family history of premature hair follicle loss) and dietary (deficiency of zinc or iron or malnutrition) [13].

Conclusions

Many aspects of PCOS diagnosis remain controversial. Even the name of this nosological concept is misleading as in fact the term „polycystic“ refers to multifollicular structure of the gonads and it has nothing to do with the presence of cysts. As we have proven, diagnosing the syndrome is complicated even if we take into account only the most important criteria specified in each of the diagnostic recommendations (ESHRE/ASRM, NICHD and AEPCOS). The problems discussed in the present publication cannot be neglected, thus it is necessary to conduct further clinical and scientific research. Further research will provide the means to develop new, precise and reliable methods of diagnosing PCOS.

In the summary it is worth to present the most important premises of PCOS diagnosis keeping in mind also the controversy mentioned herein above. First of all, we believe that it is important that the same diagnostic criteria be used by as many physicians and health care facilities as possible. ESHRE/ASRM criteria would be the best choice, since those are widely recognized. It should be remembered though that the AEPCOS guidelines may be more suitable in the future. To apply the criteria properly the methods of evaluating ovulation, hyperandrogenisation, hyperandrogenemia and ovarian morphology need to be improved. Ovulation should be evaluated in ultrasound examination and (or) by hormonal tests. To determine the severity of hyperandrogenisation accurately we should identify the severity of hirsutism (the presence of acne and hair loss are less significant) with the use of a modified Ferriman-Gallwey score. Ethnic differences should be taken into account in
diagnosing hirsutism. The selection of appropriate laboratory method to evaluate hyperandrogenemia is a controversial issue. Some studies indicate that the best method would be to measure the level of free testosterone in the serum. It is difficult to properly interpret ultrasonographic data of the ovaries, nevertheless the evaluation should follow the ESHRE/ASRM recommendations. Evaluation of the consensus of the ultrasound examination results among different observers and for the same researcher would be the optimal solution. The effort put into adequate diagnosis of PCOS will be beneficial both for the patients and clinical practitioners leading to better results of treatment of this frequently occurring disorder.

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