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ARTICLE

How to recognize PCOS: results of a web-based survey at IVF-worldwide.com

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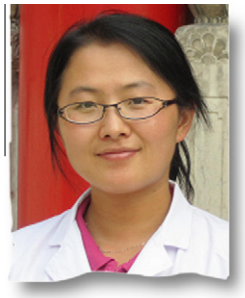

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Abstract This retrospective evaluation of a web-based survey posted from 1 to 30 September 2010 was to determine which diagnostic tools physicians are currently utilizing to diagnose polycystic ovary syndrome (PCOS). Responses from 262 IVF centres in 68 countries are included in the study. Providers used various diagnostic criteria to diagnose PCOS, including the Rotterdam criteria (82%), National Institutes of Health criteria (8%), Androgen Excess Society 2006 criteria (3%) and other classification systems (7%). Many providers utilized diagnostic tools not necessarily included in traditional classification systems: 58% of respondents evaluated LH/FSH ratio in addition to androgen concentrations to define patients with PCOS; physicians also commonly obtain measurement of anti-Müllerian hormone (22%) and impaired glucose tolerance (74%) in diagnosing PCOS. Many respondents (64%) felt that polycystic-appearing ovaries on ultrasound with anovulation and a normal serum prolactin should be adequate criteria to diagnose PCOS. In conclusion, while the majority of centres (82%) uses the Rotterdam criteria to diagnose PCOS, other criteria and diagnostic tools are commonly used in evaluating patients with suspected PCOS. This study highlights the need for continual re-evaluation of PCOS diagnostic criteria with an ultimate goal of developing a consensus definition for the disorder in the future.

KEYWORDS: androgen, diagnosis, impaired glucose tolerance, LH/FSH ratio, PCOS

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Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder with a heterogeneous constellation of clinical manifestations which primarily affects reproductive-aged women (Norman et al., 2002). This clinical heterogeneity has resulted in a challenging path to create universally accepted diagnostic criteria for PCOS. Since the disorder was first described in 1935 by Stein and Leventhal (1935), the definition of PCOS has evolved significantly. In 1990, the National Institutes of Health (NIH) established diagnostic criteria for PCOS which called for clinical and/or laboratory evidence of hyperandrogenism and oligoanovulation, with the exclusion of other causes of hyperandrogenism such as adult-onset congenital adrenal hyperplasia, hyperprolactinaemia and androgen-secreting neoplasms (Goudas and Dumesic, 1997). In 2003, another conference of experts was convened in Rotterdam, the Netherlands. The meeting recommended that PCOS be defined when two of the three following features are present: oligo- or anovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries found on ultrasound (The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group, 2004). Per the Rotterdam criteria, ultrasonographic evidence of polycystic ovaries is either by ovarian volume in one or two ovaries $>10\,cm^3$ and/or a follicle count (2–9 mm) of $\geq$12 follicles. In 2006, still another group, the Androgen Excess PCOS Society, defined the diagnostic criteria for PCOS as excess androgen activity with oligo- or anovulation and/or polycystic ovaries identified on ultrasound with the exclusion of other causes of hyperandrogenism (Azziz et al., 2006).

Superimposed on these numerous diagnostic criteria are a number of other tests that are believed to be associated with PCOS. A strong correlation exists between PCOS and metabolic syndrome (Baranova et al., 2011; Moran et al., 2010; Rahmanpour et al., 2012; Teede et al., 2010). Consequently, some have promoted evaluating patients for the presence of insulin resistance when PCOS is suspected (Baptiste et al., 2010; Panidis et al., 2012; Wongwananuruk et al., 2012). Similarly, some have advocated including measurement of the ratio of LH to FSH in the diagnostic workup of patients with suspected PCOS (Lewandowski et al., 2011a; Ma et al., 2011). These and other commonly performed tests are distinct from the standardized diagnostic criteria classically included for PCOS. Furthermore, there is disagreement as to whether the exhaustive workup for hyperandrogenism as required for diagnosis in the definitions provided by the NIH and Androgen Excess PCOS Society is practical or helpful in every patient (Lewandowski et al., 2011b).

The complex nature of PCOS has resulted in the absence of a universally accepted set of diagnostic criteria for PCOS. IVF-Worldwide (www.IVF-Worldwide.com) is a comprehensive IVF-focused website linking doctors and specialists in IVF centres around the world in order to encourage dialogue and discuss special treatments and medications. With the use of this internet-based survey tool, this study attempted to determine what diagnostic values/tools practitioners are utilizing to diagnose PCOS.

Materials and methods

Johns Hopkins Institutional Review Board (IRB) determined that the research does not involve human subject research under the regulations of the Department of Health and Human Services or the Food and Drug Administration. Consequently, formal IRB approval was not obtained. The web-based questionnaire entitled 'PCOS – definition, diagnosis and treatment' was posted on the IVF-Worldwide website on 1 September 2010 and was closed on 30 September 2010. The survey contained demographic questions including the name of the clinic's medical director, the name of the IVF unit, email address, country and number of IVF cycles performed in the unit in the most recent year. The survey evaluated the practice patterns and opinions of respondents with a series of 'yes' or 'no' and multiple-choice questions.

Quality assurance methods

During the study period, the website had an average of about 1000 entries per month (differentiation between 'professional' and 'non-professional' reviewers was not possible). In order to minimize duplicate reports from a unit and possible false data, computerized software assessed the consistency of four parameters in the self-reported data of the unit surveyed with existing data of units registered on the IVF-Worldwide website. These parameters included the name of the unit, the name of the unit director, the country and its email address. If at least three of these parameters from the survey matched the website archive data, this reporting site's data were included in the statistical analyses.

Data evaluation

The raw data used in this study, which have been not publicly available prior to this publication, were uploaded into a computerized spreadsheet using Excel (Microsoft, Redmond CA, USA). Binomial confidence intervals for proportions were calculated by the modified Wald method with significance defined as $P < 0.05$ using a DataStar software package (DataStar, Waltham, MA, USA). Incomplete surveys were excluded from the analysis.

Results

Of 309 respondents that initially began the survey, 47 failed to complete the survey and were excluded. Therefore, final surveys were evaluated from 262 centres in 68 nations. Each clinic performed an average of 684 (range 100–4500) IVF cycles annually. The global distribution of clinics was: Europe, 87 clinics (33%); Asia, 62 clinics (24%); South America, 56 clinics (21%); USA/Canada, 33 clinics (13%); Africa, 13 clinics (5%); and Australia, 11 clinics (4%). The questions and positive responses associated with definition and diagnosis of PCOS organized by the responding centres are outlined in **Table 1**.

A significant majority of respondents, 243 (93%; $P < 0.001$), agreed that reaching a clear definition of the

Table 1 Questions and answers associated with definition and diagnosis of PCOS organized by 262 centres.

Question	*Positive response*
Do you think that reaching a clear definition of the ovarian state is important for the treatment?	93 (243)
Do you define a patient with PCOS based on the Rotterdam ESHRE/ASRM consensus criteria?	92 (242)
Do you measure LH/FSH ratio and androgens to define patients with PCOS?	58 (151)
In your opinion is androgen excess a prerequisite for the definition of PCOS?	37 (96)
Should ultrasound appearance of PCO in the presence of anovulation, with normal prolactin, be enough for the definition?	64 (167)
In the workup for diagnosis would you look for non-classical congenital adrenal hyperplasia?	63 (164)
Should a definition of PCOS be important for the treatment?	85 (222)
Do you routinely measure AMH?	22 (58)
If the patient presents with anovulation and PCO on ultrasound, is the LH/FSH ratio important?	33 (87)
Do you assess for IGT?	74 (194)
Among the 74% who measured IGT:	
All patients	39 (75)
Obese patients only	61 (119)

Values are % (*n*).
AMH = anti-Müllerian hormone; IGT = impaired glucose tolerance; PCO = polycystic ovaries; PCOS = polycystic ovary syndrome.

state of ovarian function is important in treating PCOS. When asked 'do you define patients with PCOS based on the Rotterdam ESHRE/ASRM consensus criteria', 242 (92%) a significant majority ($P < 0.001$) responded 'yes'. However, when asked to further identify which set of criteria was their diagnostic tool of choice, 216 (82%), stated that they use the Rotterdam criteria in diagnosing PCOS as compared with criteria set forth by the NIH 20 (8%), Androgen Excess PCOS Society 8 (3%) or other 18 (7%). **Figure 1** illustrates the nature of PCOS diagnostic criteria preferred in different continents. Interestingly, 100% of responding units in Australia use the Rotterdam criteria, while in USA/Canada 30% of clinics adopt criteria other than the Rotterdam consensus. IVF centres from other regions, ranging from 11% to 21%, use alternative criteria, although the Rotterdam criteria are used in most centres (79–89%).

As an imperative element of PCOS, androgen assessment is inevitably included in the questionnaire. Interestingly, 166 centres (63%) did not feel that androgen excess was a prerequisite for the definition of PCOS. For the question 'which androgens do you measure?', the most commonly evaluated androgens are outlined in **Table 2**. Total testosterone (10%), free testosterone (13%), free androgen index (5%) and dehydroepiandrosterone sulphate (5%) are the top four elements in addition to measurement of the combination of androgens (60%).

In response to the question regarding other laboratory values commonly used to aid in the diagnosis of PCOS, anti-Müllerian hormone (AMH) was ordered by 58 (22%) and LH/FSH ratio and androgens were obtained by 151 (58%) of the centres. When the patient presents with anovulation and polycystic ovaries on ultrasound, 52 (20%) centres considered that LH/FSH ratio and androgen concentrations need to be measured while 35 (13%) centres would utilize LH/FSH ratio only. Many respondents (194, 74%) stated that they routinely assessed women for impaired glucose tolerance (IGT) during a PCOS workup. Of these respondents, 61% stated they would perform an IGT workup on obese patients only, while 39% stated this workup is appropriate for all women with suspected PCOS. The most common methods for evaluating IGT are illustrated in **Table 3**.

Many respondents (164, 63%) stated that they would routinely test patients for non-classical congenital adrenal hyperplasia during a PCOS evaluation. Many respondents (167, 64%) felt that polycystic-appearing ovaries on

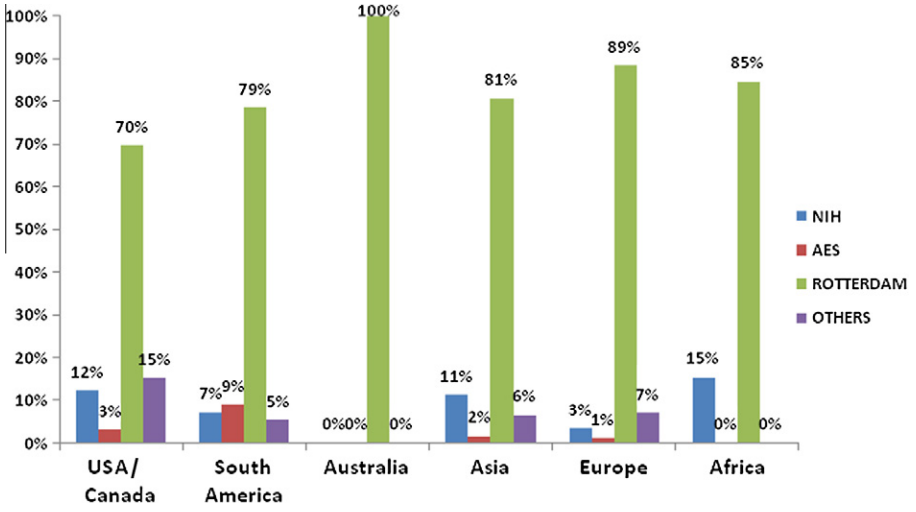

Figure 1 Preferred PCOS diagnostic criteria by continent. AES = Androgen Excess Society; NIH = National Institutes of Health.

Table 2 Measurement of androgens organized by 262 centres.

Androgen	*Positive response*
Total testosterone	10 (25)
Free testosterone	13 (33)
Free androgen index	5 (13)
Androstenedione	0 (1)
DHEAS	5 (13)
17-Hydroxyprogesterone	1 (2)
Combination of the above	60 (156)
None of the above	7 (19)

Values are % (*n*).
DHEAS = dehydroepiandrosterone sulphate.

ultrasound in the setting of anovulation and a normal serum prolactin should be adequate criteria to diagnose PCOS.

Discussion

This survey appears to be the largest study to date evaluating the practice patterns surrounding the diagnostic criteria used to clinically diagnose PCOS worldwide. However, the model of this survey is a significant departure from the traditional approach of gauging provider practice patterns. Specifically, this survey was not sent directly to providers but was instead available on an open-access basis. This novel approach was developed to gauge the practice patterns of clinics worldwide on a large scale. In this respect, this survey model was successful: this survey captured the practice patterns of 262 centres, a goal that would be exceedingly difficult with a traditional survey model.

While the methodology of this survey did result in a large sample size, there are several concerns that exist regarding the application of this survey's results to the widespread medical community. Specifically, the centres that entered data volunteered to participate and therefore an inherent self-selection bias may be present in this data. While every effort was made to ensure that multiple responses by individual clinics were not included, the possibility for such an occurrence could not be completely eliminated. Additionally, extensive laboratory testing may have been performed prior to patient referral to the IVF centre.

Table 3 Measurements for assessing impaired glucose tolerance organized by 262 centres.

Test	*Positive response*
Fasting glucose	6 (17)
Oral GTT	24 (64)
Fasting insulin (I)	6 (17)
Insulin/glucose ratio	10 (25)
HOMA-IR	7 (19)
QUICKI	1 (2)
Combination of the above	30 (79)
None of the above	15 (39)

Values are % (*n*).
GTT = glucose tolerance test; HOMA-IR = homeostasis model assessment-insulin resistance; QUICKI = quantitative insulin-sensitivity check index.

Furthermore, this survey was retrospective in nature, relying on those completing the survey to make estimates of their practice patterns rather than derive their practice patterns from objective patient data. This survey is also subject to inconstancies that are inherent to any such tool. For example, in one question, 92% of respondents stated that they used the Rotterdam criteria to diagnosis PCOS but when this same question was posed in a different manner later in the survey, the percentage of respondents stating they primarily used the Rotterdam criteria was 82%. Lastly, the survey results did not represent a global perspective in a balanced manner as more than half of all clinics hailed from either Europe or Asia while only 13% of clinics represented the USA or Canada.

The Rotterdam criteria clearly define a polycystic ovary as having ultrasonographic evidence of either ovarian volume in one or two ovaries $>10\ cm^3$ and/or a follicle count (2–9 mm) of ≥ 12 follicles. Because this criterion is widely utilized, the study assumed that questions dealing with the use of ultrasonographic diagnosis of polycystic ovaries would use this definition. However, specific questions in this survey evaluating practice patterns dealing with the use of ultrasonographic diagnosis of polycystic ovaries failed to specifically define which criteria practitioners utilized to identify an ovary as 'polycystic' and this represents a potential source of inconsistency in this data set. Furthermore, this study did not define which clinical features on physical examination, such as hair loss or acne, were accepted as evidence of androgen access. Other questions in the survey could have also been more clearly presented to respondents. For example, one question asked 'do you routinely measure AMH' with 58 (22%) of respondents answering 'yes'. However, the context of this question was not necessarily clear as it corresponds to PCOS diagnosis since many infertility clinics may order this test for other purposes such as determining ovarian reserve. Similarly, the question enquiring as to whether LH/FSH ratio is obtained to aid in the diagnosis of PCOS is also problematic in isolation. For example, this information may have been obtained more to determine probable ovarian response in the context of ovarian stimulation rather than for strictly diagnostic purposes.

Despite these limitations, this survey is a valuable adjunct to more formalized and objective estimates on this topic. Firstly, this survey represents the practice patterns of both academic centres and private practices. This is of paramount importance as the opinions of academic practitioners, particularly in the USA and Europe, may not represent the views of the larger private practice community or physicians across the world. The results of this study may be of value to societies defining diagnostic criteria in the future as this study identifies which components of the PCOS diagnostic criteria are most widely accepted. Furthermore, this survey identifies adjunctive testing that is commonly being performed to aid in identifying patients with PCOS. Similarly, these adductive tests, if being performed on a large scale, may imply that such tests should be considered by professional societies drafting future guidelines for the diagnosis of PCOS. Additionally, the

identification of commonly used diagnostic evaluations may prompt further research determining the true value of these modalities in the evaluation and treatment of PCOS.

The vast majority, 243 (93%) centres, of respondents agreed that the creation of a universally accepted set of diagnostic criteria for PCOS is an important goal. While 216 (82%) clinics cited using the Rotterdam criteria to diagnose PCOS, 46 (18%) of clinics use other diagnostic criteria. This study shows a relatively high percentage (82%) of centres that cite using one common set of criteria (Rotterdam) in the diagnosis of PCOS. This observation is certainly valuable and points to a general trend internationally to rely on the Rotterdam criteria to define PCOS. Consequently, studies evaluating questions dealing with PCOS in the future may utilize this observation to use the Rotterdam criteria confidently as the diagnostic criteria of choice given this clear international preference. However, these results also highlight the diagnostic inconsistencies from centre to centre. Additionally, a relatively large portion of respondents utilize laboratory testing not included in the major diagnostic criteria for evaluating PCOS (Rotterdam, NIH or Androgen Excess Society criteria). Serum LH/FSH ratio is commonly obtained by 151 (58%) of respondents and a IGT workup is commonly obtained by 194 (74%) of respondents.

The fact that a significant number of physicians choose to pursue further or different testing than that described within the major diagnostic criteria for PCOS may suggest a lack of consensus regarding what constitutes PCOS. Indeed, the LH/FSH ratio has long been referred to in the infertility literature as a valuable diagnostic tool for PCOS (Banaszewska et al., 2003; Ma et al., 2011; Younis et al., 2011). Additionally, the evolving understanding of the disorder's physiological basis increasingly links PCOS to the metabolic syndrome and other endocrinological disorders (Gluszak et al., 2012; Liang et al., 2012). This linkage is reflected in the present survey by the high proportion of clinics that routinely evaluate patients for IGT.

In the course of evaluating patients for PCOS, an extensive laboratory workup for hyperandrogenism is often performed (Dennedy et al., 2010; Rachon, 2012). However, in the vast majority of instances, this workup fails to identify pathological factors, such as Cushing syndrome or an androgen-producing tumour, which are either serious or easily correctable. Interestingly, 164 (63%) of respondents stated that they would not routinely test patients for non-classical congenital adrenal hyperplasia during an evaluation of PCOS. While the workup for these disorders is appropriate in patients with the 'warning signs' of moderate to severe virilization, the routine evaluation of all disorders related to androgen excess is not universally agreed upon.

Of specific interest, however, is that when asked if androgen excess is a prerequisite for the definition of PCOS, 96 (37%) of respondents chose the answer choice 'yes'. This is inconsistent with other responses on this survey, which noted that 82—92% of respondents stated that the Rotterdam criteria was their diagnostic tool of choice in diagnosing PCOS. These inconstancies are fascinating and point out opportunities for both research and education among the medical community. Other inconsistencies also exist between the ASRM/ESHRE and the responses of this survey. For example, the ASRM/ESHRE Rotterdam Report states 'it is prudent to screen obese women (BMI >27 kg/m^2) with PCOS with an oral glucose tolerance test', but only 61% of those claiming utilization of this test in this survey limited its use to obese patients (The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group, 2004). Regardless of the reason for these discrepancies, this survey highlights clear inconsistencies within common practice patterns that deserve further studies to elucidate either more accepted general diagnostic guidelines or enhanced physician education.

Additionally, the manner in which androgen excess is evaluated is not standardized, either in the diagnostic recommendations or in clinical practice, as indicated by this survey. In the opinion of some investigators, androgen excess is the *sine qua non* for the diagnosis of PCOS. However, only 80—85% of women with clinical hyperandrogenism have PCOS (Azziz et al., 2004, 2009). Androgen overexpression is reflected by clinical and/or biochemical evidence of hyperandrogenism. Clinical evidence includes such features as hirsutism (Ferriman and Gallwey, 1961), acne (Slayden et al., 2001), alopecia (Futterweit et al., 1988) and acanthosis nigricans (Schwartz, 1994). Biochemical evidence of hyperandrogenism is arrived at through serum concentrations of androgens including testosterone, androstenedione, dehydroepiandrosterone and dehydroepiandrosterone sulphate. In this survey, the majority (60%) of respondents did not rely upon one single laboratory marker and instead tested for multiple markers simultaneously.

PCOS is a complex syndrome that results in metabolic alterations that have various clinical manifestations. Since its description in the 1930s, developing a universally accepted definition for PCOS has proven an elusive goal. This study possesses significant limitations which prevent the present results from being definitively representative of the practice patterns of all reproductive endocrinology clinics. Indeed, all surveys have inherent limitations. Ultimately, a series of questions, many of which consist of simply 'yes' or 'no' questions, are inadequate to fully capsulate the practice pattern of an entire clinic. However, the strengths of this study, including its relatively large sample size and global reach, are worthy of discussion and may reflect aspects of PCOS diagnosis that deserve further attention. These data suggest that the Rotterdam criteria are by far the most widely utilized diagnostic criteria today. However, significant numbers of clinics use other criteria. Furthermore, the majority of clinics use adjunctive laboratory testing in the workup of PCOS. Given the constant evolution of the physiological understanding of PCOS, it seems reasonable that the diagnostic criteria for the disorder should also evolve with time.

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References

Azziz, R., Sanchez, L.A., Knochenhauer, E.S., Moran, C., Lazenby, J., Stephens, K.C., Taylor, K., Boots, L.R., 2004. Androgen excess in women: experience with over 1000 consecutive patients. J. Clin. Endocrinol. Metab. 89, 453—462.

Azziz, R., Carmina, E., Dewailly, D., Diamanti-Kandarakis, E., Escobar-Morreale, H.F., Futterweit, W., Janssen, O.E., Legro, R.S., Norman, R.J., Taylor, A.E., Witchel, S.F., 2006. Positions statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. J. Clin. Endocrinol. Metab. 91, 4237–4245.

Azziz, R., Carmina, E., Dewailly, D., Diamanti-Kandarakis, E., Escobar-Morreale, H.F., Futterweit, W., Janssen, O.E., Legro, R.S., Norman, R.J., Taylor, A.E., Witchel, S.F., 2009. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil. Steril. 91, 456–488.

Banaszewska, B., Spaczynski, R.Z., Pelesz, M., Pawelczyk, L., 2003. Incidence of elevated LH/FSH ratio in polycystic ovary syndrome women with normo- and hyperinsulinemia. Rocz. Akad. Med. Bialymst. 48, 131–134.

Baptiste, C.G., Battista, M.C., Trottier, A., Baillargeon, J.P., 2010. Insulin and hyperandrogenism in women with polycystic ovary syndrome. J. Steroid Biochem. Mol. Biol. 122, 42–52.

Baranova, A., Tran, T.P., Birerdinc, A., Younossi, Z.M., 2011. Systematic review: association of polycystic ovary syndrome with metabolic syndrome and non-alcoholic fatty liver disease. Aliment. Pharmacol. Ther. 33, 801–814.

Dennedy, M.C., Smith, D., O'shea, D., Mckenna, T.J., 2010. Investigation of patients with atypical or severe hyperandrogenaemia including androgen-secreting ovarian teratoma. Eur. J. Endocrinol. 162, 213–220.

Ferriman, D., Gallwey, J.D., 1961. Clinical assessment of body hair growth in women. J. Clin. Endocrinol. Metab. 21, 1440–1447.

Futterweit, W., Dunaif, A., Yeh, H.C., Kingsley, P., 1988. The prevalence of hyperandrogenism in 109 consecutive female patients with diffuse alopecia. J. Am. Acad. Dermatol. 19, 831–836.

Gluszak, O., Stopinska-Gluszak, U., Glinicki, P., Kapuscinska, R., Snochowska, H., Zgliczynski, W., Debski, R., 2012. Phenotype and metabolic disorders in polycystic ovary syndrome. ISRN Endocrinol. 2012, 569862.

Goudas, V.T., Dumesic, D.A., 1997. Polycystic ovary syndrome. Endocrinol. Metab. Clin. North Am. 26, 893–912.

Lewandowski, K.C., Cajdler-Luba, A., Salata, I., Bienkiewicz, M., Lewinski, A., 2011a. The utility of the gonadotrophin releasing hormone (GnRH) test in the diagnosis of polycystic ovary syndrome (PCOS). Endokrynol. Pol. 62, 120–128.

Lewandowski, K.C., Cajdler-Luba, A., Bienkiewicz, M., Lewinski, A., 2011b. Women with oligo-/amenorrhoea and polycystic ovaries have identical responses to GnRH stimulation regardless of their androgen status: comparison of the Rotterdam and Androgen Excess Society diagnostic criteria. Neuro Endocrinol. Lett. 32, 847–856.

Liang, S.J., Liou, T.H., Lin, H.W., Hsu, C.S., Tzeng, C.R., Hsu, M.I., 2012. Obesity is the predominant predictor of impaired glucose tolerance and metabolic disturbance in polycystic ovary syndrome. Acta Obstet. Gynecol. Scand. http://dx.doi.org/10.1111/j.1600-0412.2012.01417.x (epub ahead of print).

Ma, C.S., Lin, Y., Zhang, C.H., Xu, H., Li, Y.F., Zhang, S.C., Tan, Y., Quan, S., Xing, F.Q., 2011. Preliminary study on the value of ratio of serum luteinizing hormone/follicle-stimulating hormone in diagnosis of polycystic ovarian syndrome among women with polycystic ovary. Zhonghua Fu Chan Ke Za Zhi 46, 177–180.

Moran, L.J., Misso, M.L., Wild, R.A., Norman, R.J., 2010. Impaired glucose tolerance, type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: a systematic review and meta-analysis. Hum. Reprod. Update 16, 347–363.

Norman, R.J., Davies, M.J., Lord, J., Moran, L.J., 2002. The role of lifestyle modification in polycystic ovary syndrome. Trends Endocrinol. Metab. 13, 251–257.

Panidis, D., Tziomalos, K., Misichronis, G., Papadakis, E., Betsas, G., Katsikis, I., Macut, D., 2012. Insulin resistance and endocrine characteristics of the different phenotypes of polycystic ovary syndrome: a prospective study. Hum. Reprod. 27, 541–549.

Rachon, D., 2012. Differential diagnosis of hyperandrogenism in women with polycystic ovary syndrome. Exp. Clin. Endocrinol. Diabetes 120, 205–209.

Rahmanpour, H., Jamal, L., Mousavinasab, S.N., Esmailzadeh, A., Azarkhish, K., 2012. Association between polycystic ovarian syndrome, overweight, and metabolic syndrome in adolescents. J. Pediatr. Adolesc. Gynecol. 25, 208–212.

Schwartz, R.A., 1994. Acanthosis nigricans. J. Am. Acad. Dermatol. 31, 1–19 (quiz 20–2).

Slayden, S.M., Moran, C., Sams, W.J., Boots, L.R., Azziz, R., 2001. Hyperandrogenemia in patients presenting with acne. Fertil. Steril. 75, 889–892.

Stein, I.F., Leventhal, M.L., 1935. Amenorrhoea associated with bilateral polycystic ovaries. Am. J. Obstet. Gynecol. 29, 181.

Teede, H., Deeks, A., Moran, L., 2010. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. BMC Med. 8, 41.

The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group, 2004. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum. Reprod. 19, 41–47.

Wongwananuruk, T., Rattanachaiyanont, M., Indhavivadhana, S., Leerasiri, P., Techatraisak, K., Tanmahasamut, P., Angsuwathana, S., Dangrat, C., 2012. Prevalence and clinical predictors of insulin resistance in reproductive-aged thai women with polycystic ovary syndrome. Int. J. Endocrinol. 2012, 529184.

Younis, J.S., Jadaon, J.E., Haddad, S., Izhaki, I., Ben-Ami, M., 2011. Prospective evaluation of basal stromal Doppler studies in women with good ovarian reserve and infertility undergoing *in vitro* fertilization-embryo transfer treatment: patients with polycystic ovary syndrome versus ovulatory patients. Fertil. Steril. 95, 1754–1758.

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