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Editorial

Controversy Regarding Classification of Polycystic Ovary Syndrome (PCOS) Remains Unresolved with Newer Classifications Emerging Day by Day in the Complex Syndrome-A Short Communication

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We reviewed the diagnostic criteria of poly cystic ovary syndrome (PCOS), how they have continued to remain an issue where no consensus had been appearing and were viewed how the classifications had been increasing [1-8] (Table 1). Still it was currently agreed that the earlier 3 classifications (National Institute of Health [NIH]), Rotterdam 2003 along with the Androgen Excess and PCOS Society (AE-PCOS) [2006] can be compared, if we get insight that PCOS, the way it is currently diagnosed, can be divided further into 4 phenotypes (A-D), which has decreased the disagreement. Some of the diagnostic criteria of above classifications just have more or low phenotypes as compared to other ones (like Rotterdam 2003 takes into account all 4, while AE-PCOS 2006 considers A-C only and NIH 1990, A and B only).

Organization Group	Year	Criteria
National Institute of Health (NIH) [2]	1990	Both hyperandrogenism and chronic anovulation
Rotterdam European Society for Human [3]	2003	Two of the following conditions: hyperandrogenism, chronic anovulation, polycystic ovary
Reproductive Medicine (ASRM)-sponsored PCOS census workshop group Androgen Excess Society [4]	2009	Hyperandrogenism (central feature; biochemical or clinical) and ovarian dysfunction including infrequent or irregular ovulation or anovulation and/or polycystic ovary
Asterdam ESHRE/ASRM sponsored [5] PCOS consensus workshop [5]	2011	Different phenotypes separated by hyperandrogenism and chronic anovulation from those by ovulatory dysfunction and PCOM.
NIH endorsed based workshop [6] European Society of Endocrinology [7]	2012 2014	Maintain broad Rotterdam criteria along with specific PCOS phenotypes for each single patient esp from metabolic point of view [6] confirmed by European society of endocrinology.
Practice Guidelines of Endocrine Society [8]	2013	Use of Rotterdam criteria for PCOS diagnosis Confirmed although characteristics of specific phenotypes at diagnosis was not considered clinically needed.

Table 1

Of greater importance, although given lesser importance is that irrespective of the criteria we use, to make a diagnosis of PCOS, relies markedly on the way our definition is given as per each factor of the syndrome that sums up i) biochemical and/or clinical hyperandrogenism, ii) oligoovulation and anovulation, and iii) polycystic ovarian morphology (PCOM), and excluding other disorders which appear similar or simulate the disorder. Basically it is the way we choose to define what constitutes normal.

Recently Ahmad., *et al*. [9] tried to consider this problem with regard to PCOM. He examined 245 subjects having PCOS, where they used the NIH 1990 criteria, that is usually known as classic PCOS and does not need the presence of PCOM for establishing the diagnosis. Further they chose 756 control women from their Ovarian Aging study. They found that the ovarian volume (OV) along with the follicle number/ovary (FNPO) reduced as age progressed for both PCOS along with controls. Moreover they realized that the initial Rotterdam statements for PCOM (OV > 10 cm^3 and/or FNPO >= 25) revealed < sensitivity along with > specificity compared with each other along with age -related cutoff -levels, which increased the sensitivity and specificity to the highest level (which they calculated with the use of Youden's statistic or index).

Multiple attempts have been tried earlier as reviewed in reference 1 for giving a definition of what is normal, and subsequently, abnormal as far as diagnosis of PCOS is concerned. Many others and the group of Ricardo Azziz have tried to get more insight in what is normal for the definition of hirsutism [10], androgens in the circulation [11] and PCOM [12]. But for understanding how we can reach diagnostic cutoff values and normal ranges, we have to understand that variable ways are there and hence potentially varying results.

E.g. to get the definition of normal variations, workers need to evaluate a group of controls who have been earlier well characterized alias super controls, and with the utilization of these subjects upper as well as lower limits of what we consider normal (although with account for any inherent difference by the use of the measurement by itself). Further these researchers will examine a population and define the upper and lower cutoffs for a specific parameter with the utilization of a previously specified percentile (e.g. 95^{th} percentile as the upper normal limit). Problem is very rarely, if at all, do these biological parameters use these pre-established percentiles.

Since for almost all factors definition of a disorder will cause marked overlap in the observations in between those affected and not affected subjects, thus researchers usually try to get a cutoff that can differentiate the 2 populations in a best way. E.g. the way Ahmad., *et al*. [9] utilized, researchers might use receiver operating characteristic curve for separate populations to manage to get the cutoff that is best by which the 2 can get separated. In another way, workers can examine a big cohort of unselected subjects with the use of statistical tests, like cluster analyses, for finding the natural cutoff for a parameter which differentiates the 2 subpopulations from each other [9]. Thus, the key role for workers who are studying PCOS (or any other complex disorder) will get help from these directions i.e. they give time and energy in defining what constitutes "normal" along with the so called "normal ranges".

Further Ahmadi., *et al*'s [9] findings are stimulating otherwise also. As per their pointing that what determines PCOM (OV and FNOP) are in reality not so strict as those which have been set by both Rotterdam and AE- PCOS Society Expert recommendations. The threshold values for OV and FNPO for the whole group of women who were examined (aged 25 - 40 yrs) when utilizing Youden's index (implying maximal sensitivity and specificity) were > 6.75 cm^3 and > 13, respectively which is lower in contrast to both Rotterdam and AE-PCOS Society criteria.

Moreover Ahmad., *et al.* [9] propose that one uses a way that means one makes compromise in between sensitivity and specificity, giving the understanding that they consider the parameters that they examined, namely OV and FNPO for specific diagnostic criteria. But what we have to understand is that if we utilize a test regarding screening it better be more sensitive, although less specific parameter. If the parameter is to be used in the form of one of variety of diagnostic criterion, as in PCOS, it will be better if it has specificity, even though has lower sensitivity.

Additionally, Ahmadi., *et al*. [9] emphasize on some of the problems regarding giving a definition of proper cutoffs to be able to separate populations.

I) The age groups they had used (25 to < 30, 30 - < 35 and 35 - 40 yrs) were set before hand. But there is a probability that the true age cut offs that separate young, from older, or from oldest, might be any other values (say < 28, < 33 and < 37 yrs). Hence by utilizing limits which have been decided before the research to the evaluation of definition of upper/lower normal limits might end up in results with artifacts. Azziz R [13] proposed that what might have given better results to these authors, would have been that they conducted a cluster or similar evaluation for finding the proper "age groups" to detect variations in PCOM findings.

II) As per this publication the need of most clinical doctors is to get a cutoff value, which differentiates between subjects having a disorder from the ones who do not have the same. Hence cutoffs are basically a compromise value in view of marked overlap in the results in affected vs unaffected subjects.

III) This work emphasizes on the requirement of age -determined cutoff values, that has not been given enough weightage for particular androgen amounts [14]. Right now there is a requirement for approach being simple and rapid as far as clinical medicine is concerned, with the effect of media, internet information. Hence trying to get what one considers a complex diagnostic criteria gets in use poses much more difficulty and hence it leads to improper service to the subjects who are affected with the disorder.

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