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Prevalence, Diagnostic Criteria and Metabolic Syndrome In Various Phenotype of PCOS At SMS Medical College, Jaipur Rajasthan

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Abstract

Background- Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age.

Methods- This prospective case-control study was undertaken to assess prevalence, diagnostic criteria and metabolic syndrome in various phenotype of PCOS .216 women newly diagnosed with PCOS were classified into one of the four potential PCOS phenotypes based on history, examination and investigations.

Results- Prevalence of metabolic syndrome was maximum in phenotype B (37.5%) followed by type A (34.00%), type C (25.00%) and least in type D (17.14%).Maximum percentage of metabolic syndrome cases was found in women with age >35 years (100%) and least in women with age <24 years (15.15%).Maximum cases of metabolic syndrome were found when BMI was >35 kg/m^2 (100%) and least, when BMI was <24 kg/m^2 (6.12%).

Conclusion- This study provides evidence that endocrine and metabolic profile is deranged in all phenotypes of PCOS and the derangement is more in the hyperandrogenic phenotypes that is phenotype A, B, C as compared to non-hyperandrogenic phenotype that is phenotype D.

Keywords- Metabolic syndrome, Polycystic ovary syndrome, Phenotypes.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age. The prevalence of PCOS varies depending on the criteria used to make the diagnosis. The prevalence of PCOS among different geographic regions ranges from 5% to 10% according to NIH 1990 criteria; from 10 to 15% according to AE-PCOS 2006, from 6% to 21% when the ESHRE/ASRM 2003 criteria were applied. Current incidence of PCOS is increasing due to change in life style and stress. In India prevalence of PCOS is 2.2 to 22%.[1]

Three sets of diagnostic criterion have been proposed over the past three decades.[2–7] The first formal attempt to classify PCOS was carried out at a National Institute of Child Health and Human Development of the US **National Institutes of Health (NIH) conference, April 1990.**[2] A tabulation of participant impressions indicated that clinical or biochemical hyperandrogenism (HA) and

chronic oligo-anovulation (OA), after the exclusion of related disorders were considered key diagnostic PCOS features.

The second definition was based on the consensus opinion of 27 PCOS experts, who met in Rotterdam, the Netherlands, May 2003.[3,4] The conference was partially sponsored by the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM). As a result of this meeting, ultrasound characteristics for polycystic ovarian morphology (PCOM) were added to the NIH 1990 definition, making it more complex. **The ESHRE/ASRM 2003 PCOS criteria (ROTTERDAM)** required the presence of two of the following three findings: -

1. signs of clinical or biochemical HA
2. chronic ovulatory dysfunction (OD) and
3. PCOM, after exclusion of secondary causes[3,4].

Importantly, the introduction of Rotterdam criteria led to a substantial increase in the number of patients diagnosed with PCOS, as well as broadened the heterogeneity of PCOS phenotypes as compared with the NIH definition.[8]

Subsequently, an increasing body of evidence suggested that Hyperandrogenism seemed to be the strongest determinant of the PCOS pathophysiology and a key predictor of the associated metabolic dysfunction.[9-11] Therefore, it has been suggested that non-hyperandrogenic PCOS patients (i.e., those with chronic anovulation and PCOM) do not truly represent patients with the syndrome and are etiologically distinct from hyperandrogenic PCOS.[6,7]

In **2006 a task force assembled by the Androgen Excess & PCOS Society (AEPCOS),** composed of five investigators from the United States and six from Europe and Australia, conducted a systematic review of published literature to identify the link between PCOS phenotypes and independent morbidity. They concluded that PCOS is a disorder predominantly of androgen excess and that a concise diagnosis of PCOS should be based on the presence of clinical or biochemical HA in combination with ovarian dysfunction (i.e., OD or PCOM), excluding other disorders causing androgen excess or ovulatory dysfunctions, like congenital adrenal hyperplasia, androgen secreting tumors, Cushing syndrome, Hyperprolactinemia before diagnosing PCOS.[6,7]

Therefore, the AE-PCOS 2006 criteria excluded the non-hyperandrogenic phenotype (i.e., phenotype D, including PCOM + OD) that was proposed by the 2003 Rotterdam definition.[3,4]

The global use of varying PCOS diagnostic criteria raised issues of compatibility for PCOS research worldwide, which then resulted in confusion within clinical practice and a ‘‘delay in progress in understanding the syndrome’’.[5] Therefore, the NIH in 2012 undertook an Evidence-Based Methodology PCOS Workshop which, among other topics, addressed the ‘‘benefits and drawbacks’’ of existing diagnostic criteria.[5] The meeting was organized in accordance with standard NIH criteria for Consensus Development Programs, and all available evidence was presented by 29 PCOS experts from different countries to four workshop panel members whose research expertise was not in PCOS.[5] As a result the panel recommended the use of the broader ESHRE/ ASRM 2003 criteria, but accompanied with a detailed description of the PCOS phenotype included.[5] As previously proposed by Azziz R et al (2006)[6], the NIH consensus panel recommended use of the following phenotype classification: -

- phenotype A/Frank PCOS: HA (clinical or biochemical presence) + OD + PCOM
- phenotype B/Non-PCO PCOS: HA + OD
- phenotype C/Ovulatory PCOS: HA +PCOM and

- phenotype D/Mild and Normoandrogenic PCOS: OD + PCOM[5].

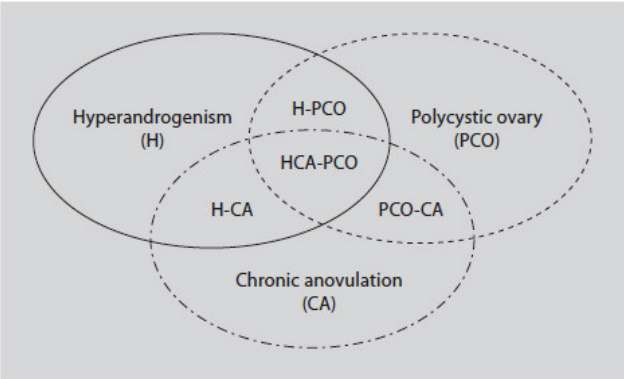

Figure-1: The different phenotypes in PCOS. Type A: hyperandrogenism, chronic anovulation and polycystic ovaries; type B: hyperandrogenism and chronic anovulation; type C: hyperandrogenism and polycystic ovaries; type D: chronic anovulation and polycystic ovaries.

The proposed NIH's 2012 phenotypic extension of the Rotterdam (ESHRE/ASRM) approach is highly convenient for clinical practice and epidemiologic research. Notwithstanding the ongoing discussion about the validity of current PCOS criteria, phenotypic classification allows for the characterization of PCOS populations according to the presence and/ or absence of key features. As long as the presence of HA, OD, and PCOM are considered the core PCOS features and are reported as such, the specific criteria (NIH 1990, ESHRE/ASRM 2003, or AE-PCOS 2006) being used to define PCOS are of limited consequence, because essentially the PCOS phenotypes are the ''building blocks'' of all existing definitions.

Evolution of the Diagnostic Criteria for Polycystic Ovarian Syndrome

Parameter	NIH 1990[2]	ESHRE/ASRM 2003[3,4]	AE-PCOS 2006[6,7]	NIH 2012 Extension of ESHRE/ASRM 2003[5]
Criteria	HA OA	HA OD PCOM	1. HA 2. Ovarian dysfunction (OD and/or PCOM)	1. HA 2. OD 3. PCOM
Limitations	1. Two of two criteria required	1. Two of three criteria required	1. Two of two criteria required	1. Two of three criteria required ; and 2. Identification of specific phenotypes included: - A : HA + OD + PCOM B : HA + OD C : HA + PCOM D : OD + PCOM
Exclusion of related or mimicking etiologies				

Note: AE-PCOS ¼ Androgen Excess & PCOS Society; ASRM ¼ American Society for Reproductive Medicine; ESHRE ¼ European Society for Human Reproduction and Embryology; HA ¼ hyperandrogenism; NIH ¼ National Institutes of Health; OA ¼ oligo-anovulation; OD ¼ ovulatory dysfunction; PCOM ¼ polycystic ovarian morphology.

The phenotypic approach would be helpful to identify those women with PCOS who are at the highest risk for metabolic dysfunction — those with ''classic'' PCOS phenotypes (i.e., phenotypes A and B)[6] and these women were informed and counselled about their present and long term health risk so they could be managed timely and accordingly. Another important application of this approach was seen when conducting epidemiologic research and clinical trials[5] and also for comparisons with other well-defined PCOS populations.

The prevalence of MetS in PCOS patients is almost twice as great as in the general population of women, raising the risk of cardiovascular disease by seven times [12]. However, the metabolic syndrome study of each PCOS phenotype reveals phenotypic groups with a worse metabolic profile and a larger number of harmful results to one's health [13]. Because of the high incidence of the association between PCOS and MetS, we sought to identify the frequency of metabolic syndrome in each PCOS phenotype and the

factors associated with metabolic risk in the population of the city jaipur,Rajasthan.

Material And Methods

Study Type

A case control prospective type of study.

Study Period

From April 2017 to Oct 2018.

Study Location

Hospital based study conducted in the department of Obstetrics & Gynaecology, S.M.S. Medical College, Jaipur.

Study Population

Study population (Infertile women of age group 18 to 38 years) was divided into two groups: -

Case- Infertile PCOS women

Control- Infertile Non PCOS Women

SAMPLE SIZE

Sample size was calculated at 90% confidence level assuming prevalence of type B PCOS in 11.37% of patient as per reference study.
A the precision of 5% (absolute allowable error) minimum 156 patients of PCOS and 50 controls were required at sample size for comparison of clinical, biochemical and other variables.

Inclusion Criteria

Case - Infertile Women of reproductive age (18-38 years) group who were willing to participate in the study, diagnose as having PCOS according to ESHRE/ASRM ROTTERDAM CRITERIA 2003.

Control – Women of the same age group visiting OPD with complaint of infertility unrelated to PCOS, thyroid or Prolactin Dysfunction.

Exclusion Criteria

Infertile Women of reproductive age (18 to 38 years) who were having: -

- Hypothyroidism,
- Hyperprolactinaemia,
- Congenital adrenal hyperplasia
- Androgenic tumors,
- Cushing disease,
- Women on medication for ≤ 6 months prior to the study eg- hormonal therapy or medication for dyslipidemia.

Statistical Analysis

Data collected was entered in MS Excel sheet. Qualitative data was expressed as proportion and percentage and Quantitative data was expressed as mean and standard deviation. Qualitative data was analysed by using χ^2 test and quantitative data was analysed by using ANOVA test and unpaired 't' test (significant was set at $p<0.05$ and highly significant at $p<0.001$).

Observation

Table – 1

Classification of Participants Using Various Criteria

Criteria	No. of Cases	%
NIH	66	32.04
Rotterdam	156	75.73
AE-PCOS Society	86	41.75

Above table shows prevalence of various diagnostic criteria in our study population. Prevalence of PCOS cases according to Rotterdam criteria was maximum that was 75.73% followed by AE-PCOS Society 41.75% and minimum in NIH criteria, that was only 32.04 % of study population

Table – 2

Prevalence of Different Phenotypes of PCOS

Phenotypes	No. of Cases	%
Phenotype A	50	32.05
Phenotype B	16	10.26
Phenotype C	20	12.82
Phenotype D	70	44.87

Above table shows the prevalence of various phenotype of PCOS. In PCOS cases, prevalence of type D phenotype was most common (44.87%) followed by type A (32.05%), type C (12.82%) and type B was least common (10.26%).

Table – 3

Prevalence of Metabolic Syndrome Among Various Phenotypes

Phenotype	No. of Cases	Metabolic Syndrome No. of PCOS Cases	% of Metabolic Syndrome Cases	p-value
Phenotype A	50	17	34.00%	0.03
Phenotype B	16	6	37.5%	
Phenotype C	20	5	25.00%	
Phenotype D	70	12	17.14%	
Controls	50	3	6.00%	

Above table shows distribution of the prevalence of metabolic syndrome among various phenotypes and controls. We compared prevalence of metabolic syndrome among various phenotype of PCOS. It was found that phenotype B had maximum prevalence (37.5%) followed by type A (34.00%), type C (25.00%) and least in type D (17.14%).

In our study the overall prevalence of metabolic syndrome in PCOS cases was 25.64% and in controls 6.00%. There was significant association seen for metabolic syndrome in PCOS cases and controls (p <0.03)

Table – 4

Distribution of Metabolic Syndrome in PCOS Cases by Age

Age Groups (years)	Total Subjects	PCOS Cases With Metabolic Syndrome	PCOS Cases Without Metabolic Syndrome	p-value
<24	66	10 (15.15%)	56 (84.85%)	0.007
25-29	71	20 (28.16%)	51 (71.84%)	
30-34	18	9 (50.00%)	9 (50.00%)	
>35	01	1 (100.00%)	0 (0.00%)	

Above table shows distribution of metabolic syndrome in PCOS cases by age. Least number of cases with metabolic syndrome were found when age group was <24 years (15.15%). On increasing the age group risk of metabolic syndrome increased so that maximum cases (100%) had metabolic syndrome when age group was >35 years. So, we concluded that on increasing the age the risk for metabolic syndrome increases and also showed statistically significant association between Age and no of Metabolic syndrome (p <0.007).

Table – 5

Distribution of Metabolic Syndrome in PCOS Cases by BMI

BMI (kg/m^2)	Total No. of Cases	PCOS Cases With Metabolic Syndrome	PCOS Cases Without Metabolic Syndrome	p-value
<24.9	49	3 (6.12%)	46 (93.88%)	0.001
25-29.9	86	17 (19.77%)	69 (80.23%)	
30-34.9	18	11 (61.11%)	7 (38.88%)	
>35	3	3 (100.00%)	0 (0.00%)	

The above table shows the distribution of metabolic syndrome in PCOS cases according to BMI. Least number of cases of metabolic syndrome were found when BMI was <24 kg/m^2 (6.12%). On increasing the BMI risk of metabolic syndrome increases so that maximum cases (100%) had metabolic syndrome when BMI was >35 kg/m^2. So, we can concluded that with increasing BMI the risk for metabolic syndrome increases and showed statistically significant correlation between BMI and prevalence of MetS (p <0.001).

Discussion

Prevalence of PCOS cases according to Rotterdam criteria was maximum that was 75.73% followed by AE-PCOS Society 41.75% and minimum in NIH criteria, that was only 32.04 % of study population.

Study conducted by Yildiz BO et al (2012)[14] reported that the prevalence was 6.1% with the NIH criteria, 15.3% using AE –PCOS criteria and 19.9% according to Rotterdam criteria.

Study conducted by Clark NM et al (2014)[15] reported 53%, 70% and 62% participants were diagnosed with NIH, Rotterdam criteria and AE and PCOS society respectively. Similar results were found in our study.

Bozdag G et al (2016)[16] conducted a study named 'systemic and meta-analysis on prevalence of PCOS according to least one subset of diagnostic criteria'. The proportions of PCOS prevalence (95% CL) according to diagnostic criteria of NIH, Rotterdam and AE-PCOS Society were 6%, 10% and 10%, respectively.

Wolf WM et al (2018)[17] study results found prevalence of PCOS in the identified population was 51% according to NIH, 83% with Rotterdam criteria, 70.6% with AE-PCOS Society.

In PCOS cases, prevalence of type D phenotype was most common (44.87%) followed by type A (32.05%), type C (12.82%) and type B was least common (10.26%).

Similar results was reported by Zhang HY et al (2013)[18] study. In which prevalence of phenotype D (52.2%) was most common followed by A (26.8%), C (13.4%) and least in B (7.6%).

Most of the studies reported that prevalence of phenotype A was most common.

While Study conducted by Chauhan S et al (2014)[19] reported that prevalence of phenotypes A, B, C and D was 23.3%, 13.3%, 52.6% and 19.5%, respectively. In which prevalence was maximum for phenotype C and least in phenotype B.

Pikee S et al (2016)[20] found prevalence of women with PCOS was maximum for phenotype C (31.28%) followed by phenotype A (20.85%), phenotype D (12.80%) and phenotype B (11.37%).

In our study the overall prevalence of metabolic syndrome in PCOS cases was 25.64% and in controls 6.00%. There was significant association seen for metabolic syndrome in PCOS cases and controls ($p < 0.03$).

Hyperinsulinemia and IR are thought to be key pathological factors for PCOS and metabolic syndrome. Maximum number of cases of hyperinsulinemia and IR were present in classic phenotypes (A, B), so maximum prevalence of metabolic syndrome was seen in phenotype B, A and intermediate in phenotype C and least in phenotype D. Our study suggested that non hyperandrogenic PCOS (phenotype D) represent a form of PCOS associated with milder metabolic profile compared to the other phenotypes (A, B, C).

Prevalence of metabolic syndrome was 19.2% in study conducted by Chauhan S et al (2014)[19] and 15.9% according to Goverde AJ et al (2009)[20] using Rotterdam consensus criteria.

Kar S (2013)[21]study reported overall prevalence of metabolic syndrome to be 35.07%. Hyperandrogenic phenotype B (50%) and A (37.04%), had significantly higher prevalence of metabolic syndrome than non-hyperandrogenic phenotype D (10%) (p-value ≤ 0.001).

Similar results were also found in Bil E et al (2016)[22] study. Prevalence of metabolic syndrome was higher in phenotypes A and B (29.6% and 34.5%) compared with other phenotypes C and D (10.0% and 8.3%; $p<0.001$). Both studies correlate with our findings.

Shroff R et al (2007)[23] study results showed the age adjusted prevalence of metabolic syndrome to be 36.1% for women with phenotype A (O+H+P) (OR 6.3), 41.3% for women with phenotype B (H+O) (OR 7.8), 42.3% for women with phenotype C (H+P) (OR 8.2). For these three phenotypes, the prevalence of metabolic syndrome was significantly higher than controls (8.3% $p<0.001$). The age adjusted prevalence of metabolic syndrome in women

with phenotype D (O+P) 20.3% was not statistically different compared with the control subjects (p<0.14%).

Conclusion

This study provides evidence that endocrine and metabolic profile is deranged in all phenotypes of PCOS and the derangement is more in the hyperandrogenic phenotypes that is phenotype A, B, C as compared to non-hyperandrogenic phenotype that is phenotype D. The hyperandrogenic phenotypes have more severe risk of metabolic syndrome as compared to non-hyperandrogenic phenotype.

References

1. Nidhi R, Padmalatha V, Nagarathna R, Amritanshu R. Prevalence of polycystic ovarian syndrome in Indian adolescents. J Pediatr Adolesc Gynecol. 2011 Aug; 24(4) : 223-7.
2. Zawadzki JK, Dunaif A. Diagnostic criteria for polycystic ovary syndrome; towards a rational approach. In: Dunaif A, Givens JR, Haseltine F, Merriam G, editors. Polycystic ovary syndrome. Boston: Blackwell Scientific; 1992.
3. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004; 81 : 19–25.
4. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004; 19 : 41–7.
5. National Institutes of Health. Evidence-based methodology workshop on polycystic ovary syndrome, December 3-5, 2012. Executive summary. Available at: https://prevention.nih.gov/docs/programs/pcos/FinalReport.pdf. Accessed March 1, 2016.
6. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Positions statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. J Clin Endocrinol Metab 2006; 91 : 4237–45.
7. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril. 2009; 91 : 456–88.
8. Broekmans FJ, Knauff EA, Valkenburg O, Laven JS, Eijkemans MJ, Fauser BC. PCOS according to the Rotterdam consensus criteria: change in prevalence among WHO-II anovulation and association with metabolic factors. BJOG. 2006; 113 : 1210–7.
9. Rosencrantz MA, Coffler MS, Haggan A, Duke KB, Donohue MC, Shayya RF, et al. Clinical evidence for predominance of delta-5 steroid production in women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2011; 96 : 1106–13.
10. Georgopoulos NA, Papadakis E, Armeni AK, Katsikis I, Roupas ND, Panidis D. Elevated serum androstenedione is associated with a more severe phenotype in women with polycystic ovary syndrome (PCOS). Hormones (Athens). 2014; 13 : 213–21.
11. Carmina E, Chu MC, Longo RA, RiniGB, Lobo RA. Phenotypic variation in hyperandrogenic women influences the findings of abnormal metabolic and cardiovascular risk parameters. J Clin Endocrinol Metab. 2005; 90 : 2545–9.
12. Wang ET, Kao CN, Shinkai K, Pasch L, Cedars MI. Phenotypic comparison of Caucasian and Asian

women with polycystic ovary syndrome: a cross-sectional study. FertilSteril,2013; 100: 214-218.

13. Dokras A. Cardiovascular disease risk factors in polycystic ovary syndrome. Semin Reprod Med,2008; 26: 39-44.
14. Yildiz BO, Bozdag G, Yapici Z, Esinler I, Yarali H. Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria. Hum Reprod. 2012; 27 : 3067–73.
15. Clark NM, Podolski AJ, Brooks ED, Chizen DR, Pierson RA, Lehotay DC, Lujan ME. Prevalence of Polycystic Ovary Syndrome Phenotypes Using Updated Criteria for Polycystic Ovarian Morphology: An Assessment of Over 100 Consecutive Women Self-reporting Features of Polycystic Ovary Syndrome. Reprod Sci. 2014 Aug; 21(8) : 1034-1043.
16. Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod. 2016 Dec; 31(12) : 2841-2855.
17. Wolf WM, Wattick RA, Kinkade ON and Olfert MD. Geographical Prevalence of Polycystic Ovary Syndrome as Determined by Region and Race/Ethnicity. Int J Environ Res Public Health. 2018; 15(2859) : 1-13
18. Zhang HY, Guo CX, Zhu FF, Qu PP, Lin WJ, Xiong J. Clinical characteristics, metabolic features, and phenotype of Chinese women with polycystic ovary syndrome: a large-scale case-control study. Arch Gynecol Obstet. 2013 Mar; 287(3) : 525-31.
19. Chauhan S, Joshi B, Mukherjee S et al. A cross-sectional study of polycystic ovarian syndrome among adolescent and young girls in Mumbai, India. Indian J Endocrinol Metab. 2014; 18(3) : 317-24.
20. Pikee S, Shivani S, Jayshree B. Endocrine and Metabolic Profile of Different Phenotypes of Polycystic Ovarian Syndrome. J Obstet Gynaecol India. 2016 Oct; 66(Suppl 1) : 560-6.
21. Kar S. Anthropometric, clinical, and metabolic comparisons of the four Rotterdam PCOS phenotypes: A prospective study of PCOS women. J Hum Reprod Sci. 2013 Jul; 6(3) : 194-200.
22. Bil E, Dilbaz B, Cirik DA, Ozelci R, Ozkaya E, Dilbaz S. Metabolic syndrome and metabolic risk profile according to polycystic ovary syndrome phenotype. J Obstet Gynaecol Res. 2016 Jul; 42(7) : 837-43.
23. Shroff R, Syrop CH, Davis W, Van Voorhis BJ, Dokras A. Risk of metabolic complications in the new PCOS phenotypes based on the Rotterdam criteria. Fertil Steril. 2007 Nov; 88(5) : 1389-95.