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Clinical, Hormonal and Metabolic Profile of Different Phenotypes of Polycystic Ovarian Syndrome

Neeti Mahala[1], Seema Sharma[2*]

[1]Resident (MS), [2*]Professor, Department of Obstetrics & Gynaecology,
Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India.

ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is one of the most frequently encountered hormonal disorder with metabolic abnormalities in females that can present at puberty, during reproductive age or even after menopause. Therefore, the aim of this study was to evaluate the occurrence of different phenotypes among PCOS women and to compare the hormonal assay and metabolic profile of different phenotypes of PCOS.

Materials & Methods: The present study was an observational study conducted on 160 women of the age group of 16-35 years and diagnosed with PCOS, in the department of obstetrics and Gynecology at Mahatma Gandhi Medical College and Hospital, Jaipur from January 2017 to July 2018. Diagnosis of PCOS was done by using the ESHRE/ASRM criteria and subjects were divided into 4 phenotypes by using the all probable combination of Rotterdam criteria. Hirsutism was assessed by using Modified Ferriman Gallwey score. Score <8 - Normal, 8-15- Mild and >15 indicate moderate to severe hirsutism.

Results: 160 PCOS women were distributed in 4 phenotypes and the most prevalent phenotype was phenotype D, 40.63% followed by 32.50% phenotype A and 14.38% phenotype C. Mean age of overall women was 24.94±4.86. In this study overall prevalence of metabolic syndrome was 37.5%. Almost

50% women of phenotype A had metabolic syndrome followed by 35% of phenotype B, 34.78% of phenotype C and least prevalence was in phenotype D 30.77%.

Conclusion: We concluded that the most prevalent phenotype is nonhyperandrogenic phenotype 40.63% and least common phenotype is classic nonpolycystic ovaries phenotype (12.50%).

Keywords: Polycystic Ovarian Syndrome (PCOS), Phenotype, Harmonal, Metabolic.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the most frequently encountered hormonal disorders with metabolic abnormalities in females that can present at puberty, during reproductive age or even after menopause. High variability among the observers is seen in the incidence of PCOS ranging from 2.2 % to 26 % in India which may be due to different sets of definition evolved through the time.[1,2]

Rotterdam criteria for diagnosis of PCOS include the presence of any two of the following criteria: clinical or biochemical hyperandrogenism, polycystic ovaries on ultrasonography, anovulation or oligomenorrhea.[3] On the basis of the most widely used definition, 4 different phenotypes have been identified for PCOS diagnosis using the possible combination of Rotterdam criteria. Other than major criteria of Rotterdam, PCOS patients may present clinically with the manifestations of acne, hypomenorrhea, hair loss and inability to conceive.[4]

The clinical features of PCOS are diverse and can influence welfare and health-related standard of living[5], additionally it can cause cardiovascular complications and metabolic syndrome (MetS) in future. All these clinical feature and complications varies among phenotypes. Cause and underlying pathophysiology of PCOS is still unclear as there is no single starting point for the development of PCOS but hypothalamic-pituitary axis plays an important role in pathogenesis. Hyperandrogenism is a key feature of PCOS and increase in level of androgen is both adrenal and ovarian origin. Metabolic abnormalities of PCOS include an increase in insulin level, obesity and abnormal level of lipoprotein. IR leads to an increase in insulin level which increases the chances of hyperglycemia and type 2 DM in later life.[6,7] Therefore, the aim of this study was to evaluate the occurrence of different phenotypes among PCOS women and to compare the hormonal assay and metabolic profile of different phenotypes of PCOS.

MATERIALS AND METHODS

The present study was an observational study conducted on 160 women of the age group of 16-35 years and diagnosed with PCOS, in the department of obstetrics and Gynecology at Mahatma Gandhi Medical College and Hospital, Jaipur from January 2017 to July 2018.

Diagnosis of PCOS was done by using the ESHRE/ASRM criteria and subjects were divided into 4 phenotypes by using the all probable combination of Rotterdam criteria.

- Phenotype A with hyperandrogenism (H) + oligomenorrhea (O) + polycystic ovaries on USG (P)
- Phenotype B with hyperandrogenism (H) + oligomenorrhea (O)
- Phenotype C with hyperandrogenism (H)+ polycystic ovaries on USG (P)
- Phenotype D with oligomenorrhea (O)+ polycystic ovaries on USG (P)

A detailed clinical history and clinical examination were done in all the patients. Clinical history included the detailed menstrual, personal, past, family, marital and obstetric history followed by complete general examination.

Hirsutism was assessed by using Modified Ferriman Gallwey score. Score <8 - Normal, 8-15- Mild and >15 indicate moderate to severe hirsutism. BMI was body weight in kilograms divided by height in meter square. The hormonal analysis was done on Day 2 or 3 of menstruation which included Serum LH, Serum FSH, LH/FSH ratio, Serum estradiol, Total testosterone levels, Serum prolactin and Serum TSH. For the diagnosis of metabolic syndrome harmonized (2009) criteria was used. For that BP, Waist circumference, Fasting blood sugar, Triglyceride and High density lipoprotein measured. Exclusive criteria were Pregnancy, Thyroid disorder, Hyperprolactinemia, Adrenal hyperandrogenemia, Cushing's disease and DM.

Statistical Analysis

The clinical, hormonal and metabolic profile of different phenotypes of PCOS were compared and data were presented as mean ± SD. One way ANOVA was used for the values which followed a normal distribution and nonparametric Kruskal–Wallis test was used for the values that did not follow the normal distribution. Multiple intergroup values comparison was done by using Bonferroni test and for comparison of phenotype association with metabolic syndrome univariate logistic regression was used. Comparison of percentages of different groups was calculated using the Chi square test. Significance was set at $P<0.05$. For statistical analysis, SPSS was used.

Table 1: Clinical parameter of 4 phenotypes of PCOS

Parameters	Phenotype A	Phenotype B	Phenotype C	Phenotype D	P value
Prevalence	52 (32.50%)	20 (12.50%)	23 (14.38%)	65 (40.63%)	
Age	25.52±4.51	23.7±4.37	25±5.36	24.85±5.12	0.56
FG score	12.98±4.55	11.30±2.52	14.43±5.47	3.48±1.48	0.0001
BMI	24.46±4.977	24.73±3.410	25.28±4.177	24.70±3.451	0.603
WC	80.08±16.33	79.60±9.48	75.80±11.22	81.46±11.72	0.288
Systolic BP	119.35 ±8.554	122.30 ±9.652	120.87±15.408	118.09±10.797	0.373
Diastolic BP	76.31±7.602	80.10±8.179	78.26±9.191	77.09±7.850	0.153

Table 2: Hormonal parameters of 4 Phenotypes of PCOS

Parameters	Phenotype A	Phenotype B	Phenotype C	Phenotype D	P value
LH (mIU/ml)	9.93±6.36	8.56±6.17	8.12±4.20	7.02±4.25	0.076
FSH (mIU/ml)	6.88±4.55	5.76±1.12	6.85±1.40	5.65±1.25	0.034
LH/FSH	1.39±0.73	1.53±1.17	1.19±0.60	1.24±0.69	<0.001
Testosterone(ng/dl)	69.06±56.94	58.55±29.80	64.65±50.35	9.82±8.26	<0.001

Table 3: Metabolic parameters of 4 Phenotypes of PCOS

Parameters	Phenotype A	Phenotype B	Phenotype C	Phenotype D	P value
HDL (mg/dl)	47.85±10.24	50.40±8.07	50.26±11.35	54.08±10.08	0.301
Triglyceride	124.62±23.59	135±38.08	115.87±22.80	111.31±25.43	0.002
FBS (mg/dl)	90.17±25.34	87.25±14.15	92.30±25.62	84.95±15.74	0.365

Table 4: Prevalence of metabolic syndrome among 4 Phenotypes of PCOS

MetS	Phenotype A		Phenotype B		Phenotype C		Phenotype D		Total
	No	%	No	%	No	%	No	%	
Present	25	48.08	7	35	8	34.78	20	30.77	60
Absent	27	51.92	13	65	15	65.22	45	69.23	100
Total	52	100.00	20	100.00	23	100.00	65	100.00	160

RESULTS

160 PCOS women were distributed in 4 phenotypes and the most prevalent phenotype was phenotype D, 40.63% followed by 32.50% phenotype A and 14.38% phenotype C. Least prevalent phenotype was phenotype B and only 12.50% PCOS women belonged to this phenotype. Mean age of 160 women was 24.94±4.86 and Mean age of all 4 phenotypes was almost similar. 25.52±4.51, 23.7±4.37, 25±5.36 and 24.85±5.12 was Mean±SD of phenotype A, B, C and D respectively.

Clinical Profile

Among the 4 phenotypes of PCOS, maximum overweight women belonged to phenotype A 40.38% followed by 35.38% in phenotype D, 34.78% in phenotype C and only 25% in phenotype B. In Phenotype A, B, C and D women with normal BMI were 51.92%, 65%, 52.17% and 60% respectively. Women with WC >80 cm were maximum in phenotype A 36.54% and least in phenotype C 13.04%. There was no significant difference in waist circumference among the phenotypes. Modified FG score was highest in phenotype C 14.43±5.47 followed by 12.98±4.55 in phenotype A, 11.30±2.52 in phenotype B and lowest in phenotype D 3.48±1.48. Highest prevalence 26.09% of systolic BP >130mmHg in phenotype C followed by phenotype B, D and A 20%, 13.85% and 9.62% women in decreasing order. Phenotype B had the highest 30% women of DBP >85mmHg followed by 26.09%, 15.38% women in phenotype C, D respectively and phenotype A women had the least prevalence 9.62%.

Hormonal Profile

All 4 phenotypes had an abnormal level of testosterone, LH and LH/FSH ratio but vary in severity. Women with raised LH level were maximum in phenotype A 30.77% followed by phenotype B 25%, phenotype D 18.46% and only 13.05% women of phenotype C. Women with increased LH/FSH ratio were maximum in phenotype A 21.15% followed by 20%, 13.85% in phenotype B, D and least in phenotype C 13.04%. While comparing testosterone level, high level of testosterone was maximum in phenotype A 53.85% followed by phenotype C and B subsequently 43.48% and 35%. In phenotype D all women had serum testosterone level in normal range. There was highly significant P<0.001 difference in the level of testosterone among the phenotypes.

Metabolic Profile

Level of serum HDL and triglyceride were significantly higher in all 4 phenotypes. Women with HDL<50mg/dl were maximum in phenotype A 46.15% and least in phenotype D 27.69%. High TG level was highest in phenotype B 20% followed by 15.38% in phenotype A, 9.23% in phenotype D and least in phenotype C 8.7%. Phenotype A had the highest number of women (17.31%) with FBS>100mg/dl followed by 10% women in phenotype B, 8.7% in phenotype C and least 6.15% in phenotype D.

Metabolic Syndrome

Table 4 shows the presence of metabolic syndrome among the phenotypes. In this study overall prevalence of metabolic syndrome was 37.5%. Almost 50% women of phenotype A had metabolic syndrome followed by 35% of phenotype B, 34.78% of phenotype C and least prevalence was in phenotype D 30.77%.

DISCUSSION

The present study was carried out in the Department of Obstetrics and Gynaecology, Mahatma Gandhi Medical College and hospital on 160 PCOS women with the aim to compare the different phenotypes of PCOS according to their clinical, hormonal and metabolic characteristics. In our study maximum, PCOS women belonged to phenotype D 40.63% followed by phenotype A 32.50%, phenotype C 14.38% and least common phenotype was B 12.50%. According to Sheena Shobti et al,[8] most common phenotype was phenotype A 45.5% and least common was phenotype B 14.4%. Wijeyaratne et al,[9] found out that maximum women belonged to phenotype A 54.6% and least common was phenotype C 7.7%. Normohyperandrogenic phenotype women were maximum in our study because these women are often symptomatic with irregular cycles and phenotype B women are mostly asymptomatic and unlikely to present in gynaecology OPD. Irregular menses was the most common complaint among the PCOS women which was complaint of 97 women out of 160. 2nd most common complaint was the inability to conceive in 24.38% women followed by excessive hair growth in 9.38% women and 5.63% women complained of acne but most of the women presented with multiple complaints.

Ramanand et al[10] did a study on 120 women for 18 months for clinical characteristics of PCOS and found irregular menses was the complaint of almost 65% of women.

On comparing the PCOS women for age 65% (maximum) women were belonged to 21-30 years age group with mean age 24.94 ± 4.86%. In all 4 phenotypes, there was not much difference in mean age with P value 0.56 which is not significant.

Olgierd Głuszak et al,[11] did a study on 93 PCOS women and found out mean age was 23.7% without much difference in each phenotype. This finding is similar to our study and according to Wijeyaratne et al[9] mean age was also 25 years.

BMI of phenotypes was compared and we found that out of 160, 91 women BMI was normal and 42% women overweight and obese women. These obese women were maximum in phenotype A 48.07% followed by 47.82%, 39.98% and 35% in phenotype C, D and B respectively.

According to Baldani et al,[12] BMI was in phenotype A, B, C and D respectively 24.5±5.3, 24.3±4.2, 25.5±4.7 and 23.3±4.1. Chae et al,[13] and Sharami et al,[14] also reported the same result.

While comparing the WC Women with WC >80 cm was maximum in phenotype A 36.54% and least in phenotype C 13.04%. WC mean ±SD in phenotype A was 80.08±16.33 and phenotype C was 75.80±11.22 with P value 0.368 (not significant).

According to Pikee et al,[15] WC>80cm in phenotype A, B, C and D were respectively in 36.36%, 33.33%, 14.81% and 28.78% women. Olgierd Głuszak et al,[11] found WC (cm) of phenotype A, B, C and D were 81 ± 14.6, 86.4 ± 14, 81.1 ± 13.3 and 87.8 ± 13.08. In most of these studies, there was no difference in WC among the phenotypes. For assessing the hirsutism modified FG Score was used. FG score less than 8 was considered normal. Women with FG score >15 that indicates severe hirsutism was maximum in Phenotype C and overall FG score was also highest in phenotype C with mean ±SD was 14.43±5.47 and least in phenotype D 3.48±1.48 that indicates a significant difference in FG score in between the phenotypes. Praveen et al[16] did a study on 120 patients of age 16-40 and reported that women with the highest FG score belonged to phenotype A and the lowest value in phenotype D. Wijeyaratne et al,[9] study showed the highest FG score mean in phenotype C 12±6 followed by phenotype A and B

and least in phenotype D 4±2. While comparing the metabolic profile of phenotypes, In our study 26.09% women of phenotype C had systolic BP >130 mmHg followed by 20%, 13.85% and 9.62% women of phenotype B, D and A. Overall 15% women had systolic BP >130 mmHg and 16.8% women had diastolic BP >85 mmHg. Out of 4 phenotypes maximum 30% women of phenotype B and least 9.62% women of phenotype A had diastolic BP> 85mmHg.

According to Shroff et al,[17] women with BP> 130/85 mmHg in phenotype A, B, C and D were subsequently 24.5% , 24.3%, 27.0%, 11.8%. Total serum testosterone level >80 ng/dl in 45 (28.12%) women. Expect phenotype D, other 3 phenotypes serum testosterone level were high. SD± mean was 69.06±56.94, 58.55±29.80, 64.65±50.35 and 9.82±8.26 with significant difference among phenotypes. (P=0.001)

According to Zhang et al,[18] total testosterone in phenotype A, B, C and D was 89 ± 29, 88 ± 33, 79 ± 16 and 38 ± 16, findings are similar to our study.

On comparing the hormonal levels in our study we found LH level> 10mIU/ml maximum in 30.77% women of phenotype A, 25% women of phenotype B, 13.05% women of phenotype C and 18.46% women of phenotype D. Mean±SD was 9.93±6.36, 8.56±6.17, 8.12±4.20 and 7.02±4.25.

Olgierd Głuszak et al[11] also did a comparative study and found that the level of LH was maximum in phenotype B and least in phenotype D. LH/FSH ratio was maximum in phenotype B 1.53±1.17 and least in phenotype C 1.19±0.60. Olgierd Głuszak et al,[11] LH/FSH ratio similar in phenotype A and B and least in phenotype D. All these hormonal investigations suggested that the high level of Testosterone and LH is maximum in classical phenotype and other studies all confirmed the same findings. There was a significant difference in the level of TG among the phenotypes. (P =0.002) and Mean± SD in phenotype A, B, C and D was respectively 124.62±23.59, 135.30±38.08, 115.87±22.80 and 111.25±43.

In our study, PCOS women with HDL level <50mg/dl was maximum in phenotype A 46.15% and least 27.69% in phenotype D. HDL mean level was almost similar among phenotypes.

Another component of metabolic syndrome was fasting blood sugar that was highest in phenotype C 92.30± 25.62 and lowest in phenotype D 84.95±15.74. Shroff et al,[17] FBS in phenotype A,B,C and D were 92± 13, 97± 26, 97± 30 and 89 ±10. All these studies suggest there is not any significant difference in the level of FBS among the phenotypes. Prevalence of metabolic syndrome in this study was 37.5%. Almost half of the women of phenotype A had metabolic syndrome and least affected women with metabolic syndrome belonged to phenotype D.

Shroff et al,[17] observed that prevalence of age-adjusted metabolic syndrome was 36.1% in phenotype A, 41.3% in phenotype B, 42.3% in phenotype C and least prevalence in phenotype D 20.3%. There was a significant difference in the prevalence of MetS among the phenotypes. All these findings suggest the prevalence of metabolic syndrome is more in hyperandrogenic phenotypes compared to non-hyperandrogenic phenotypes.

There was a slight variation in results of studies due to the heterogeneity of phenotype, in addition, variation in ethnicity, genetic and environmental factors affect the results. Results also depend upon the study group from where the patients are selected from endocrine, infertility, medicine, dermatology or gynaecology OPD.

CONCLUSION
This study suggests that there is a significant difference in various parameters of the hormonal and metabolic profile of different phenotypes of PCOS. Among the phenotypes, there was no significant difference in mean age, BMI, WC, level of FSH, LH, HDL and blood glucose and a significant difference in modified FG score, LH/FSH ratio, level of testosterone and triglyceride.

In our study, Phenotype without hyperandrogenism is the milder phenotype of PCOS with least prevalence of metabolic dysfunction. That's why all 3 hyperandrogenic phenotype needs close surveillance to prevent the long-term health implication. So, It is important to counsel properly for present and long-term health effects of PCOS in women with hyperandrogenic phenotype.

REFERENCES
1. Gill H, Tiwari P, Dabadghao P. Prevalence of polycystic ovary syndrome in young women from North India: A Community-based study. Indian Journal of Endocrinology and Metabolism. 2012;16 (Suppl 2):S389-S392.

2. Mandrelle K, Kamath MS, Bondu DJ, Chandy A, Aleyamma T, George K. Prevalence of metabolic syndrome in women with polycystic ovary syndrome attending an infertility clinic in a tertiary care hospital in south India. Journal of Human Reproductive Sciences. 2012;5(1):26-31.

3. Laven JS, Imani B, Eijkemans MJ and Fauser BC. New approaches to PCOS and other forms of anovulation. Obstet Gynecol Surv 2002; 57,755–67.

4. Teede, H, A Deeks, and L Moran. Polycystic Ovary Syndrome: A Complex Condition with Psychological, Reproductive and Metabolic Manifestations That Impacts on Health across the Lifespan. BMC Medicine 8 (2010): 41. PMC. Web. 26 July 2018.

5. Ching HL, Burke V, Stuckey BG. Quality of life and psychological morbidity in women with polycystic ovary syndrome: body mass index, age and the provision of patient information are significant modifiers, Clin Endocrinal (Oxf), 2007, 66; 373-79.

6. Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK and Imperial J (1999) Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. Diabetes Care 22,141–46.

7. Legro RS, Kunselman AR, Dodson WC and Dunaif A (1999) Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. J Clin Endocrinol Metab 84,165–69.

8. Sobti S et al. Metabolic syndrome and insulin resistance in PCOS phenotypes. Int J Reprod Contracept Obstet Gynecol. 2017 Nov;6(11):5067-73.

9. Chandrika N.Wijeyaratne, Ruwanthi de A. Seneviratne et al. Phenotype and metabolic profile of South Asian women with polycystic ovary syndrome (PCOS): results of a large database from a specialist Endocrine Clinic. Human Reproduction. 2011; 26(1): 202–13.

10. Sunita J. Ramanand, Balasaheb B. Ghongane, Jaiprakash B. Ramanand, Milind H. Patwardhan, Ravi R. Ghanghas, Suyog S. Jain. Indian J Endocrinol Metab. 2013 Jan-Feb; 17(1): 138–45.

11. Olgierd Głuszak,Urszula Stopinska-Głuszak, Piotr Glinicki, Renata Kapuscinska, Hanna Snochowska, Wojciech Zgliczynski, and Romuald Debski. Phenotype and Metabolic Disorders in Polycystic Ovary Syndrome. ISRN Endocrinology.2012; 1- 7.

12. Dinka Pavicic Baldani, Lana skrgatic, Velimir Simunic, Gordan Zlopasa, Tomislav canic and Iva Trgovcic. Characteristics of Different Phenotypes of Polycystic Ovary Syndrome Based on the Rotterdam Criteria in the Croatian Population. Coll. Antropol. 2013; 37(2): 477–82.

13. Soo Jin Chae, Jin Ju Kim, Young Min Choi, Kyu Ri Hwang, Byung Chul Jee, Seung Yup Ku, Chang Suk Suh, Seok Hyun Kim, Jung Gu Kim1 and Shin Yong Moon. Clinical and biochemical characteristics of polycystic ovary syndrome in Korean women. Human Reproduction. 2008; 23(8): 1924–31.

14. Seyedeh Hajar Sharami, Zahra Abbasi Ranjbar, Forozan Milani, Ehsan Kezem-Nejad, Afagh Hassanzadeh Rad, and Seyedeh Fatemeh Dalil Heirati The Relation between Diverse Phenotypes of PCOS with Clinical Manifestations, Anthropometric Indices and Metabolic Characteristics. Acta Medica Iranica. 2016; 54(2): 134-39.

15. Saxena Pikee, Singh Shivani, Bhattacharjee Jayshree. Endocrine and Metabolic Profile of Different Phenotypes of Polycystic Ovarian Syndrome. The Journal of Obstetrics and Gynecology of India. 2016; 66(S1):S560–S566.

16. Praveen D, Animesh M, Chandra SS, et al. Evaluation of metabolic, hormonal and clinical parameters in different phenotypes of polycystic ovary syndrome: an observational study from a tertiary care centre in Eastern India. J Diabetes Metab Disord Control. 2018;5(6):195–200.

17. Rupal Shroff, Craig H. Syrop, William Davis, Bradley J. Van Voorhis, and Anuja Dokras. Risk of metabolic complications in the new PCOS phenotypes based on the Rotterdam criteria. Fertility and SterilityVol. 88, No. 5, November 2007; 1389- 95.

18. HY Zhang, FF Zhu, J Xiong, XB Shi, SX Fu, Characteristics of different phenotypes of polycystic ovary syndrome based on the Rotterdam criteria in a large-scale Chinese population. BJOG 2009;116:1633–39.