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Original research article

COMPARISON OF PCOS PHENOTYPES AMONGST YOUNG WOMEN ATTENDING A TERTIARY CARE HOSPITAL, BASED ON THEIR CLINICAL PRESENTATION, METABOLIC AND HORMONAL PROFILE

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Abstract

Objectives: Polycystic ovarian syndrome is the most common endocrinopathy having health implications, in the present and future health of young women. Hence, our objective was to compare different polycystic ovarian syndrome (PCOS) phenotypes based on their clinical presentations, metabolic and hormonal profile of young PCOS affected women, so as to manage and counsel them in an appropriate manner.

Material and Methods: This is a cross-sectional observational study conducted amongst young women aged between 15 to 30 years attending the gynecology out-patient department. 125 PCOS patients were further divided into four phenotypes based on the National Institute of Health Consensus Panel criteria and then evaluated upon their clinical presentation, metabolic profile, hormonal profile and ovarian ultrasound features.

Results: Majority of women (58.4%) attained menarche between 13-15 years of age. The most common presenting complaint was found to be menstruation related, followed by infertility. The most prevalent phenotype was type A (40.8%) followed by type C (28.8%), type D (18.4%) and type B (12.8%) respectively. Phenotype C was found to have higher significant weight and HbA1C values; however there was no significant difference between body mass index and waist hip ratio. No significant differences were found in fasting insulin, OGTT, HOMA-IR and fasting blood sugar. Phenotype B had the highest serum Testosterone level and higher fasting insulin.

Conclusion: In the light of the present study it is recommended to screen all PCOS phenotypes, specially the younger age group, for glucose intolerance and other metabolic derangements and hence motivate or direct them towards preventive and

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treatment modalities.

Keywords: PCOS, menstrual irregularity, hormonal imbalance, glucose intolerance

Introduction

The most common endocrinopathy among women of reproductive age group is Polycystic ovarian syndrome (PCOS) [1]. The PCOS syndrome is associated with various metabolic disturbances along with a wide spectrum of clinical features like menstrual abnormalities, obesity, infertility, dyslipidemia, hyperandrogenism, insulin resistance, type 2 diabetes mellitus and metabolic syndrome [2]. However, these signs and symptoms vary widely over time [1]. The incidence of PCOS among infertile women shows that about 20% of infertility is attributed to anovulation caused by PCOS [2] and 90-95% of women seeking treatment for infertility have PCOS [3]. PCOS is not a discrete or specific endocrine disorder having a unique cause or pathophysiology, rather it is a heterogeneous disorder that is best approached as a diagnosis of exclusion [1]. This condition is relatively common in women of reproductive age group and affects 5-10% of women worldwide [4]. The diverse manifestations of polycystic ovary syndrome begins at an early age when a girl is maturing into a young woman. Hence it is important to make an early diagnosis, in order to prevent early and late sequel of this syndrome. Some of the women who develop cardiovascular disease, hypertension and endometrial cancer later in life, appear to have PCOS in their early years [2]. Upon further evaluation PCOS is characterised by chronic anovulation, oligomenorrhea, hyperandrogenism and polycystic ovary morphology on pelvic ultrasound. Some other conditions such as congenital adrenal hyperplasia, androgen secreting tumours, hyperprolactinemia, and thyroid disorder may also lead to oligo/anovulation, along with or without androgen excess, thus sharing overlapping clinical features that mimic PCOS. Even in the presence of limited studies of PCOS in India, the observational studies made by endocrinologists, gynaecologists and dermatologists show the diverse nature of PCOS phenotypes.

Several diagnostic criteria's for PCOS such as -Rotterdam's criteria, European society of Human reproduction and Embryology(ESHRE) and American Society of Reproductive Medicine(ASRM) sponsored PCOS Consensus Workshop Group 2004 are present [5]. The diagnosis of PCOS in adolescent girls can be challenging as many symptoms of PCOS mimic the normal physiologic responses of puberty. As noted, adolescents frequently have irregular menses, and acne is common [6]. Diagnosis in adolescent girls requires presence of both oligo-anovulation and hyperandrogenism [6]. Ultrasound is not required in girls less than 8 years of age after menarche due to high antral follicle count which is normal in this age group [7, 8]. In adolescence, transabdominal rather than transvaginal pelvic sonography is generally used, where image resolution is poorer.

The prevalence of obesity and diabetes mellitus in India is on the rise owing to urbanization and sedentary lifestyles [9]. The available evidence indicates that in most countries, 20-25% of the adult population have metabolic syndrome [10]. They are twice as likely to die from and three times as likely to have a heart attack or stroke when compared to people without the syndrome [11].

Because of differences in the diagnostic criteria employed, prevalence estimates vary widely, ranging from 2.2% to as high as 26% [12]. The prevalence of PCOS when

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diagnosed by the Rotterdam criteria was over twice that found when the National Institutes of Health (NIH) criteria, when used to diagnose PCOS among other approved criteria's [13].

In view of the prevalence of various presentations of PCOS, this endeavor was undertaken to compare different polycystic ovarian syndrome (PCOS) phenotypes based on their clinical presentation, metabolic and hormonal profiles among young PCOS women attending a tertiary care hospital.

Materials and Methods

In the present observational cross-sectional study, conducted from January 2021 to June 2022, 125 women of reproductive age group, between 15-30 years age with PCOS (as per Rotterdam criteria) were recruited after giving written and informed consent, keeping in line with the inclusion and exclusion criteria (Table 1). Detailed clinical history including an evaluation of menstrual cycle disturbance and/or duration of infertility was obtained. Physical examination to assess height, weight, waist and hip circumference and BMI was done. Thyroid gland and breast was examined for any abnormalities. Blood pressure was also measured. Signs of androgen excess were looked for such as- acne, alopecia, hirsutism and degree of terminal hair growth on nine regions of the body using the modified Ferriman-Gallwey scoring system (1) and recorded. Serum markers of metabolic syndrome including lipids (Total cholesterol, Triglycerides, HDL and LDL) and Haemoglobin A1C were recorded. Along with it fasting glucose and fasting insulin level was also measured. All women underwent a standard oral glucose tolerance test, performed after an overnight fasting and blood glucose was measured after 2 hours of 75g glucose ingestion. Serum endocrine markers LH, FSH, AMH, Prolactin and TSH were also evaluated. A trans-vaginal ultrasound scan was performed (at least one ovary or more in volume > $10cm^3$ and/or at least one ovary with 12 or more follicles with each follicles measuring 2-9 mm in diameter).

Table 1: Inclusion and exclusion criteria for participants included in the study.

Inclusion criteria	Exclusion criteria
▪ Age 15-30 year ▪ Minimum two criteria or all of the following (As Rotterdam criteria)	▪ Age<15 year and >30 year ▪ Smokers and alcoholics ▪ The patients with known hepatic and renal diseases. ▪ Subject with other aetioglogies of androgen excess and anovulatory infertility such as thyroid disorder, hyperprolactenemia and congenital adrenal hyperplasia ▪ Pregnant women ▪ Subjects taking antiepileptic drugs, steroid, antipsychotic drugs. ▪ Those who have used combined oral contraceptives, lipid lowering agents or Insulin sensitizer with in the last 3

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	months. ▪ Anorexia nervosa/Bullimia nervosa

Statistical analysis

Data collected was analyzed using SPSS/PC (Statistical package for the social science Inc. version 13) statistical package. Simple distribution of study variables and cross tabulation was applied. Data were entered in Microsoft excel sheet. The statistical analysis was done by using SPSS 25. Data were summarized by routine descriptive statistics by calculating percentage and mean with standard deviation. Study variables were compared using fisher exact test and chi square test and p value <0.05 was considered statistically significant.

Result

As per this single hospital based cross-sectional observational study carried among 125 PCOS women the phenotype A (40.8%) is the most common phenotype. Table 2 is showing the distribution and percentage of variables of clinical history and dermatological ultrasound findings and phenotypes. The comparison of clinical presentation of various PCOS phenotypes has been shown in Table 3. In the study population of sample size 125, the comparisons of anthropometric parameters of various phenotypes and the comparison between their metabolic and hormonal profile has been shown in Table 4 and Table 5 respectively.

Table 2: Table showing the distribution and percentage of variables of clinical history and dermatological ultrasound findings and phenotypes

Variables		Number	Percentage
Age (years)	15-20	29	23.2
	21-25	40	32
	26-30	56	44.8
Age at menarche (years)	10-12	45	36
	13-15	73	58.4
	≥16	7	5.6
Presenting complaints	Menstrual irregularity	89	71.2
	Primary infertility	36	28.8
	Secondary infertility	8	6.4
	Hirsuitism	26	20.8
Menstrual history	Regular menstruation	36	28.8
	Oligomenorrhea	75	60
	Amenorrhea	62	49.6
	Heavy menstrual bleeding	51	40.8
Dermatological findings	Acanthosis nigricans	22	17.6
	Acne	34	27.2
	Alopecia	30	24
	Hirusitism	26	20.8

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Distribution of Polycystic ovarian morphology in ultrasound	Present	108	86.4
	Absent	17	13.6
	Total	125	100
Phenotypes in PCOS	Phenotype A (OA+HA+PCO)	51	40.8
	Phenotype B (HA+OA)	16	12.8
	Phenotype C (HA+PCO)	36	28.8
	Phenotype D (OA+PCO)	23	18.4

Table 3: Comparison of clinical presentation of various PCOS phenotypes

Comparision	**OA+HA+PCO**	**OA+HA**	**HA+PCO**	**OA+PCO**	**P Value**
Total number	51 (40.8%)	16 (12.8)	36 (28.8)	23 (18.4%)	__
Age	24.03±4.02	21.4±4.91	24.36±3.80	23.63±4.81	0.136
Age of menarche	13.11±2.06	13.26±1.5	13.38±1.80	13.36±1.7	0.971
Hirsuitism	12 (22.2%)	1 (6.25%)	8 (22.2%)	0	__
Primary infertility	14 (25.9%)	2 (12.5%)	16 (44.4%)	2 (9.09%)	__
Secondary infertility	3 (5.55%)	3 (18.75)	2 (5.55%)	3 (13.6%)	__
Alopecia	12 (23.1%)	4 (25%)	13 (36.1%)	0	
Acne	21 (41.1%)	6 (37.5%)	7 (19.4%)	0	

Table 4: Comparision of anthropometric parameters of various phenotypes in study population (n=125)

Comparision	**OA+HA+PCO (n=51) Mean± std. dev**	**OA+HA (n=16) Mean ± std. dev**	**HA+PCO (n=36) Mean± std. dev.**	**OA+PCO (n=23) Mean± std. dev.**	**P Value**
Weight (in kg)	64.05±8.97	56.81±8.48	64.58±7.28	65.13±10.65	0.02*
BMI	26.42±4.16	23.4±4.48	25.83±3	26.68±4.25	0.053
Waist Circumference	87.45±7.56	84.4±8.48	85.02±4.43	85.7±5.68	0.25
HIP Circumference	99.54±7.00	95.73±9.02	95.69±7.01	97.77±6.63	0.07
Height (In feets)	5.17±0.271	5.18±0.156	5.23±0.177	5.1±0.139	0.443
Waist Hip ratio	0.87±0.04	0.875±0.04	0.87±0.04	0.87±0.05	0.95

*Statistically significant

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Table 5: Comparision of metabolic and hormonal profile of various PCOS phenotypes among study population (N=125)

	OA+HA+PCO (n=51) Mean± std. dev	OA+HA (n=16) Mean± std. dev	HA+PCO (n=36) Mean ±std. dev	OA+PCO (n=23) Mean± std. dev.	P Value
SBP	123.84±11.54	122.6±10.12	123.36±11.23	119.54±10.64	0.49
DBP	83.31±9.18	77.93±9.88	79.63±8.74	77.59±8.97	0.03*
OGTT(2 HR)	132.54±30.95	129.8±16.55	135.63±35.71	119.2±18.46	0.21
FBS	94.58±24.05	92.13±10.66	93±32.74	91.45±9.82	0.95
HbA1C	5.6±0.72	5.31±0.49	5.63±0.78	5.2±0.51	0.004*
Fasting insulin	7.94±8.64	11.02±14	8.90±9.08	8.9±10.69	0.76
Homa-IR	7.80±8.97	7.96±6.96	9.38±12.78	11.02±13.19	0.67
LH (Baseline)	7.44±3.29	6.70±2.34	8.81±6.54	6.92±3.35	0.28
FSH (Baseline)	5.66±1.82	6.02±1.81	5.96±2.06	5.77±2.17	0.87
AMH	5.82±2.61	6.87±3.41	6.34±3.08	4.91±2.40	0.154
Serum tag	137.74±39.83	145.93±41.29	139.88±44.50	121.18±38.54	0.25
SERUM LDL	87.54±25.87	95.4±41.82	90.52±24.46	89.09±16.12	0.7
SERUM HDL	56.60±13.11	59.13±14.69	60.19±15.39	57.86±16.06	0.71
Serum testesterone	1.28±0.55	1.35±0.56	1.115±0.55	0.725±0.32	0.0003*
Total cholestrol	201.49±37.02	204.66±37.02	202.44±42.16	198.04±29.87	0.95

Discussion

In this study population, most of women were between age group 26-30 year (44.8%) followed by 21-25 year (32%) which is similar to the observations done by Abdulrazak H. Alnakash *et al.* [21] where majority(59.81%) belonged to 25-30 year age group. In this study population, mean age of menarche was 13.28±1.87 years which is similar to the findings of Joshi B *et al.*'s community based cross-sectional study of Mumbai [14], where the mean age at menarche was approximately 13 years. The most common dermatological finding was acne (27.2%) followed by alopecia (24%) which is corresponding to study by Anjum S. *et al.* [14] where acne and alopecia were found in 33 (21.5%) and 24 (15.6%) participants. This is in contrast to the observations of study Dr. Mohammad Abeed keen *et al.* [15] of Jammu and Kashmir who documented the prevalence of hirsutism, acne, female pattern hair loss and acanthosis nigricans in 78%, 48%, 31% and 30% participants. In the present study population 24% had male pattern baldness which was also in agreement to ValsinkiChristodoulopoulou *et al.* [16] where 36% of the sample had alopecia. In this study population hirsutism was 20.8% of study sample which is in contrast to a Pakistani study [15] where hirsutism was noted in 52.3% participants. Total 44 (35.2%) individuals of this study population were suffering from infertility which was comparable with the study of Anjum *et al.* [14] where infertility was (32.6%) of study sample and 37.1% was also reported in study done by Bello FA *et*

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al. [17]. Another study by Arpitha K J *et al*. [18] documented 51% of study population having infertility.

Mean BMI in this study population was 25.91±3.98 kg/m2 which did not correspond to study done by Anjum *et al.* [14] which observed mean of 31.68±7.37 kg/m2. In this present study population was 36.8% were overweight and 19.2% were obese. This finding is similar to the study done by Joshi *et al.* 's community based cross-sectional study of Mumbai [13] who reported 71.8% non-obese, 7.5% overweight, and 20.7% as obese women. Valsinki Christodoulopoulou *et al.'s* prospective observational study also showed similar finding where 15.1% of women were overweight and 24% were obese [16]. In this study, mean waist hip ratio of sample population was 0.87±0.04 which is similar to study by Yadav *et al*. [19] where mean waist hip ratio was 0.87±0.05. In my study population most common PCOS phenotype was the full-blown PCOS (Phenotype A) which includes all three features-hyperandrogenism, irregular cycles and PCOS on ultrasound with a prevalence of 40.8% (51 patients). The prevalence of phenotypes B, C, and D were 12.8% (16 patients), 28.8% (36 patients), and 18.4% (23patients) respectively. The current study results are very much similar to the study done by Welt CK *et al*. [20], were phenotype A (71%) had highest prevalece. In this study population BMI of phenotype A, B, C and D were 26.42±4.16, 23.4±4.48 kg/m^2, 25.83±3 kg/m2 and 26.68±4.25 kg/m^2 which was also statistically significant. A similar study done by Garima Sachdeva *et al*. [21] where BMI mean was 27.78±3.79 kg/m^2, 27.33±2.93 kg/m^2, 29.59±3.41 kg/m^2 and 25.83±4.79 kg/m^2 also statistically significant. In this study sample no significant differences were noted in different PCOS phenotypes while making comparison between waist circumference, waist hip ratio, 2 hr OGTT and fasting blood sugar which was similar to study done by Sachdeva G *et al*. [21].

In current study population mean Systolic BP of phenotypes A, B, C and D was 123.84±11.54, 122.6±10.12, 123.36±12.23 and 119.54±10.64 mmHg which was statistically insignificant similar to study done by C. K. Welt *et al*. [20]. Mean diastolic BP of phenotypes A, B, C and D in my study population was 83.31±9.18, 77.98±9.88, 79.63±8.76 and 77.59±8.97 mmHg which is statistically significant value P value ≤0.05, but this is not statistical significant with P value=0.126 in study of Sachdeva G *et al*. [21] where mean diastolic BP 75.18±5.75, 72.78±4.60, 74.97±5.62 and 71.67±4.08 mmHg in phenotype A, B, C and D respectively. In present study the mean of fasting insulin in phenotype A, B, C and D were 7.94±8.64, 11.02±14, 8.90±9.08 and 8.9±10.69 mIU/ml which was comparable with the study done by Olgierd Gluszrak *et al*. [22] done in Poland which had fasting insulin of phenotype A, B, C and D were 7.67±5.67, 9.71±4.39, 8.25±3.33 and 8.50±6.36 mIU/ml respectively. In this study population phenotype B had higher fasting insulin in comparison with other phenotypes and statistically non-significant and similar to the study done by Garima Sachdeva and Shalini Gainder *et al*. [21] where Phenotype B had higher insulin and HOMA-IR values than phenotypes C and D, but the results were not statistically significant (p> 0.05).

In present study population there is no difference of fasting hyperglcemia between different phenotypes, which is comparable with the study done by Welt C K *et al*. [20] in which there was no difference in the prevalence of impaired fasting glucose four groups phenotypes.

In this study population mean difference of LH, FSH in different PCOS phenotypes is statistically not significant which is similar to Garima Sachdeva *et al*. [21] observations.

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In current study population testosterone was found highest in OA + HA and lowest in OA+PCOM and was statistically significant. Similarly, in a study done J. Adams, G. Arason *et al*. [20] in which Testosterone was highest in women with OA + HA, intermediate in women with HA + PCOM, and lowest in women with OA+PCOM, was also statistically significant. The mean difference of AMH in different PCOS phenotype is statistically not significant in my study sample which is in contrast to the study done by Garima Sachdeva *et al*. [21] where mean difference is statistically significant with P value=0.035.

Conclusion

In this study population phenotype B had higher fasting insulin in comparison with other phenotypes and the most common PCOS phenotype in this study was phenotype A which includes all three features- irregular cycles, hyperandrogenism and PCOS on ultrasound. Phenotype D had significant correlation with body weight. Phenotype C had significant correlation with HbA1c and Phenotype B had significant correlation with serum testosterone.

Thus, PCOS is a common condition prevailing in women with young reproductive age group which leads to number of co-morbidities and cardiovascular atherosclerotic diseases. In the light of present study observations it is recommended to screen all the PCOS women even the younger age group for metabolic derangements and glucose intolerance. It is imperative for us clinicians to adequately stress on dietary modification, weight reduction and healthy life style behaviours to these patients to prevent cardiovascular and other complications in future life.

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