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Prevalence and Phenotypic Diversity of PCOS in Indian Women: An Observational Study

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Abstract: ***Aim and objectives: This prospective observational study aimed to investigate the prevalence and phenotypic variations of Polycystic Ovary Syndrome PCOS among Indian women aged 15-35 years, utilizing Rotterdams criteria from 2003 and to study the association between different phenotypes of PCOS and obesity. Methodology: A total of 671 women presenting with irregular menses, clinical hyperandrogenism, or polycystic ovarian morphology were evaluated with help of clinical, biochemical and radiological modality over six months. The study identified four standard PCOS phenotypes A, B, C, D and examined their associations with age, BMI, hirsutism, acne, menstrual irregularities, infertility, and various metabolic and endocrine characteristics. Results: The prevalence of PCOS was highest for phenotype A(HPO;52.57), followed by phenotype D(OP;20.97), phenotype C (HP;15.07), and phenotype B(HO;11.39).PCOS phenotypes exhibited significantly altered endocrine and metabolic profiles compared to controls, with hyperandrogenic phenotypes showing the highest risk for future metabolic disorders. Conclusion: This study underscores the need for vigilant monitoring of women with hyperandrogenic PCOS phenotypes.***

Keywords: PCOS, Indian women, Phenotypic diversity, Prevalence, Rotterdam criteria

Abbreviations: oligo and/or an ovulation (O), hyperandrogenism (H), polycystic ovary morphology (P), ESHRE: European society for human reproduction and embryology. ASRM: American society for reproductive medicine. PCOS (polycystic ovarian syndrome), DM (Diabetes mellitus), OPD (Outpatient department), PCOM (Polycystic ovarian morphology), FBG(Fasting blood glucose), IR(Insulin resistance),OGTT(Oral glucose tolerance test), HOMA-IR(Homeostasis model assessment for IR

1. Introduction

Polycystic ovarian syndrome (PCOS) is one of the most common reproductive endocrinological disorders with a broad spectrum of clinical manifestations affecting about 6-8% of women of reproductive age group (1). Globally, prevalence estimates of PCOS are highly variable, ranging from 2.2% to as high as 26% (2,3,4). Most prevalence studies in India are in hospital set-ups and recently a few studies among adolescents in schools report prevalence of PCOS as 9.13% to 36%(5,6).Clinical and biochemical features of these women may vary according to race, ethnicity, and criteria used for diagnosis (7). Common clinical presentations of polycystic ovarian syndrome include abnormal facial and skin hair growth (hirsutism), acne, and irregular or absence of menstrual periods (8).Diagnosis of PCOS continues to be controversial primarily because of the heterogenous nature of the condition which may change during the lifetime of the woman. Currently, the commonest criteria used for diagnosis of PCOS is the "Rotterdam's criteria" Rotterdam (ESHRE/ASRM)/2003:which includes any two of the following three features:1) Oligo/anovulation (O) 2) Clinical and/or biochemical hyperandrogenemia (H) 3) Polycystic ovaries on ultrasound (P), with exclusion of other known disorders of hyperandrogenemia. This generates four different phenotypes: Group A) P + H + O (PCOS complete),Group B) H+ O, Group C) H + P Group D)O+P (11).PCOS is an enigma as its underlying pathophysiology is not fully understood. Insulin resistance is thought to be the uniting pathogenic factor in the associations between hypertension, glucose intolerance, obesity, lipid abnormalities and coronary artery disease, which together constitutes metabolic syndrome or syndrome 'X.' The determinants of polycystic ovarian syndrome have been linked to both hereditary and environmental factors(5).The attributed hereditary factors include early age of sexual maturation and family history of PCOS among first-degree relatives (5,9). Studies have reported an earlier age at diagnosis of PCOS (9–12 years) among adolescent females with earlier maturation of sexual characteristics compared to their later counterparts (13–18 years) (9). This has been attributed to an increased androgen secretion associated with early onset of puberty.

2. Need for study

The prevalence of metabolic syndrome and IR in PCOS has been studied in very few different populations and ethnic groups. Also, there are limited data on differences between various phenotypes with respect to long-term metabolic risk. Especially the newer phenotypes generated by the Rotterdam criteria are inadequately studied and reported. No treatment is a panacea, because treatments, so far, have been directed at the symptoms but not at the syndrome itself. Extensive efforts should be made to fully investigate the syndrome in order to make therapy more successful and to delay the serious long term effects of the disease on patients' health. Emphasis of management is shifting from symptomatic management to lifetime management with increasing focus on long term effects of PCOS like diabetes mellitus, hypertension, infertility and uterine malignancy.

Hypothalamus

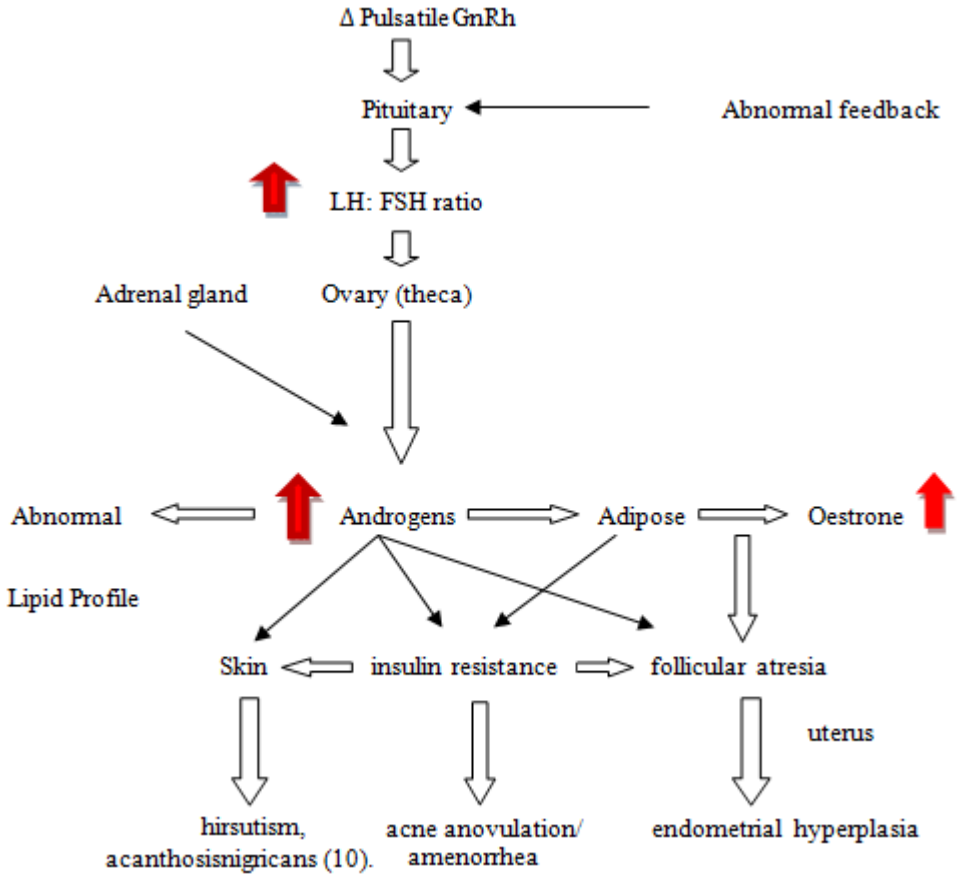

Figure 1: Flow chart showing pathophysiology of PCOS

Aims and Objectives

Aim: To determine proportion of different phenotypes of PCOS in women of age group (15-35 yrs) as defined by the Rotterdam's criteria.

Objectives:
1) To determine proportion of different phenotypes of PCOS in Indian women of age group (15-35 yrs) as defined by Rotterdam's criteria
2) To study association between different phenotypes of PCOS and obesity

3. Material and Methods

Study Site: Patients presenting to the various outpatient departments of Tertiary care Institute

Study Population: The target population will be the women of age group (15-35yrs) meeting the inclusion criteria of the study

Sample Size: A total of 671 women in reproductive age group will be included in the study.

Study Design: A Prospective Observational Study.

Study Duration: for a period of 6 months

Inclusion Criteria: Women between 18-35 yrs of age with -
1) Menstrual irregularities (oligo/ amenorrhea/ menorrhagia) and/ or
2) Signs of clinical Hyperandrogenism- hirsutism, severe acne, male pattern baldnessAnd/ or
3) PCOM on USG

Exclusion Criteria:- Patients with - Pregnancy, Hypothyroidism, Hyperprolactinemia, Adrenal Hyperandrogenemia, Cushing's disease, Severe kidney or liver disease.

3.1 Methodology

All women with a history of menstrual irregularities and clinical signs of hyperandrogenism like acne or hirsutism, h/o excess weight gain, hair loss, as per inclusion criteria were enrolled in the study from the gyanaecology, endocrinology, infertility, dermatology outpatient clinic. Patients fulfilling at least two out of three Rotterdam Consensus revised diagnostic criteria of PCOS (2003) were recruited as PCOS patients after obtaining consent. A detailed history was taken.Clinical studies were conducted on 2nd day of menses after a spontaneous or progestins induced menstrual flow in oligomenorrheic patients at 8 a.m., after overnight fasting for 10-12 hrs, blood samples were obtained. The same day a pelvic ultrasound examinations were performed by trained Radiologist, were not aware of patients endocrine profiles. Women were then stratified into 4 phenotypes as: Group A, Group B, Group C and Group D. Endocrine and metabolic differences in all groups were then studied. All findings were recorded on a predesigned proforma and the data was analysed by application of appropriate statistical tests.

Statistical Methods

Statistical analysis will be carried out with the help of SPSS (version 20) for Windows package (SPSS Science, Chicago, IL, USA).

4. Results

Out of total 671 patients evaluated in various OPD'S, 544 (81.07%) subjects satisfied Rotterdam's criteria for diagnosis of PCOS and 127 (18.93%) did not satisfy the same, hence they were taken as controls. Out of total 671, 228 were married (33.98%) while 443 were unmarried (66.02%). Out of 671 patients, 38.15% and 35.17% patients were belonged to ≤20 yrs group and 21-25 yrs group while only 4.33% patients belonged to >30 yrs of age. This suggested maximum prevalence of PCOS was in younger population. Out of total population studied, irregular menses (81.97%) was the most common presenting symptom followed by weight gain (57.53%) followed by acne(48.44%) and hirsutism (47.39%). Infertility was present in 112 patients out of 228 married patients (49.12%). Out of 544 PCOS patients, family history of DM and hypertension was present in 37(5.5%) and 12 (1.9%) patients respectively where none of the control had family history of DM and only 1 had family history of hypertension. Group A had highest number of patients with raised BP (11.5%) followed by groups D (12.3%), C (7.3%) and B(1.6%).Out of 671 patients, acanthosisnigricans was found in 153 patients (22.8%)**.** Group A followed by group D had maximum patients with acanthosisnigricans. Hyperandrogenic PCOS which includes groups A, B, C had maximum patients with significant F-G score than controls and group D. Out of 544 patients, 151 patients had abnormal WC which is significant. Risk of metabolic syndrome is 2.29 (C.I.-1.44-4.28). Group A, B, D had highest number of patients with abnormal WC. Out of 544 patients, 77 PCOS patients had abnormal blood glucose than controls which is highly significant. Group A had maximum number of patients with abnormal FBS. Out of 544 patients, 111 PCOS patients had abnormal LH/FSH ratio than controls which is highly significant. Group A(34%) had maximum number of patients with abnormal LH/FSH ratio.

Table 1: Distribution of occurrence of phenotypes of PCOS

Meeting Criteria for PCOS	Number of patients	Percentage (%)
GROUP A	286	52.57
GROUP B	62	11.40
GROUP C	82	15.07
GROUP D	114	20.96
Total	544	100.0

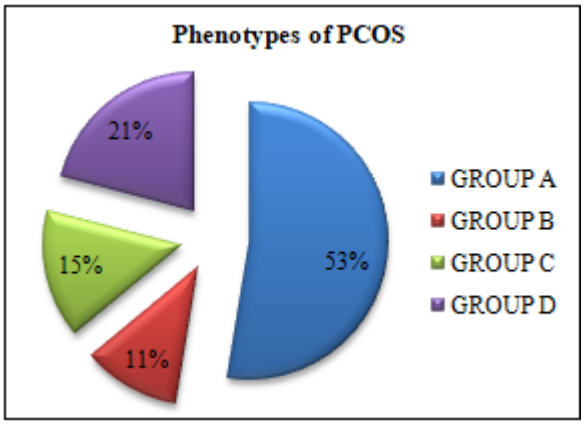

Figure 2: Frequency of occurrence of phenotypes of PCOS

Out of 544 PCOS patients who satisfied Rotterdam's criteria , group A was the most common phenotype with 52.57% occurrence followed by group D (20.96%), group C (15.07%) and group B (11.4%). (Table 1, Figure no.2**)**

Table 2: Distribution of phenotypes of PCOS and controls patients according to age groups

Age group	PCOS phenotyes				Controls
	Group A	Group B	Group C	Group D	
≤ 20	110(38.46)	14(22.58)	6(7.32))	19(16.67)	107(84.25)
21 - 25	86(30.07)	34(54.84)	55(67.07)	42(36.84)	19(14.96)
26 - 30	77(26.92)	14(22.58)	21(25.61)	38(33.33)	0
> 30	13(4.55)	0	0	15(13.16)	1(0.79)
Total	286(100)	62(100)	82(100)	114(100)	127(100)

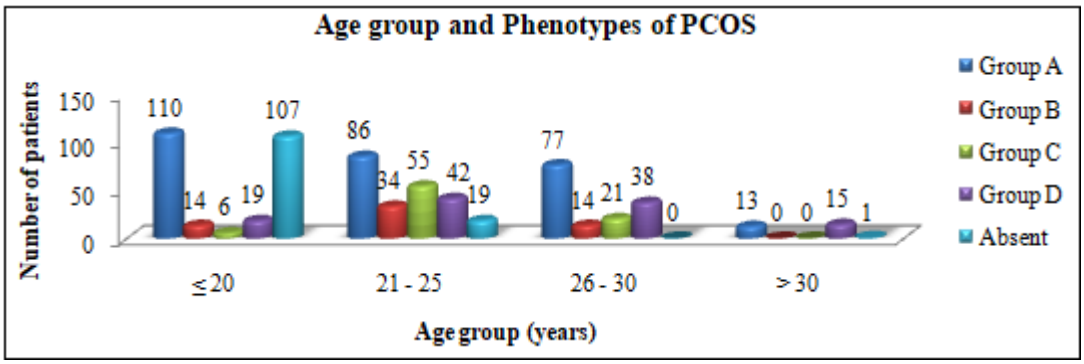

Figure 3: Frequency distribution of phenotypes of PCOS and Controls patients according to age groups

Table no. 2, Figure no.3 showed that group A (38.46%) and controls (84.25%) were maximum in ≤20 yrs group while groups B (30.07%), C (54.84%) and D (67.7%) were maximum in 21-25 years age group

Table 3: Distribution of phenotypes of PCOS and controls according to presenting symptoms

Symptoms	PCOS phenotypes				Controls
	Group A	Group B	Group C	Group D	
Irregular Menses	286(100)	62(100)	0	114(100)	88(69.29)
Hirsutism	216(75.52)	34(54.84)	55(67.07)	0	13(10.24)
Acne	189(66.08)	48(77.42)	55(67.07)	0	33(25.98)
Hair loss	131(45.8)	19(30.65)	55(67.07)	0	13(10.24)
Weight gain	200(69.93)	41(66.13)	47(57.32)	40(35.09)	58(45.67)
Infertility	52(18.18)	0	14(17.07)	46(40.35)	0

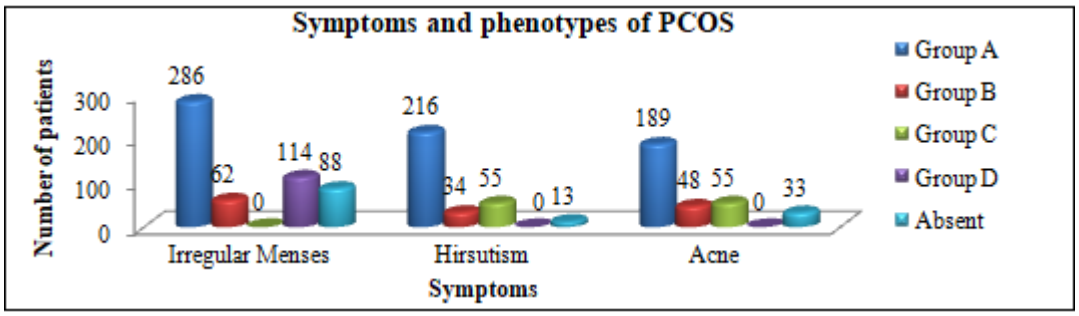

Figure 4: Frequency distribution of PCOS phenotypes and controls according to symptoms(part-I)

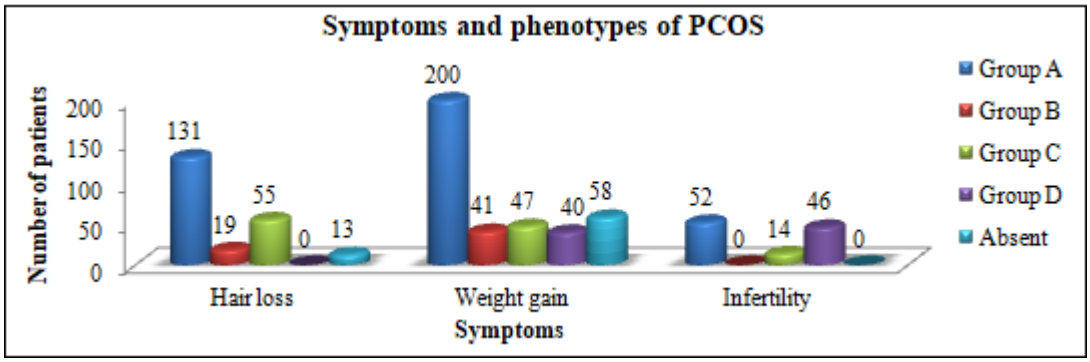

Figure 5: Frequency distribution of PCOS phenotypes and controls according to symptoms (part-II)

Symptoms of irregular menses, hirsutism, acne, hair loss, history of weight gain were statistically significant for PCOS patients as given in table no.3. symtoms of acne, hirsutism, hair loss were maximum in hyperandrogenic phenotypes (groups A, B and C) while weight gain and infertility are more common in group D. Irregular menses were present in all patients of groups A, B, D.

Table 4: Comparison of types of menstrual irregularities in PCOS phenotypes and controls

Type of Cycle	PCOS phenotypes				Controls	Total	P value
	Group A	Group B	Group C	Group D			
Oligomenorrhea	236(82.6)	56(90.3)	0	98(86)	65(51.3)	455(67.8)	<0.001
Amenorrhea	23(8.1)	1(1.6)	0	6(5.3)	17(13.3)	47(7)	
Menorrhagia	27(9.4)	5(8.1)	0	10(8.7)	9(7.1)	51(7.6)	
Normal	0	0	82(100)	0	36(28.3)	118(17.5)	
Total	286(100)	62(100)	82(100)	114(100)	127(100)	671	

p-value< 0.05 (Significant) Chi-square test used

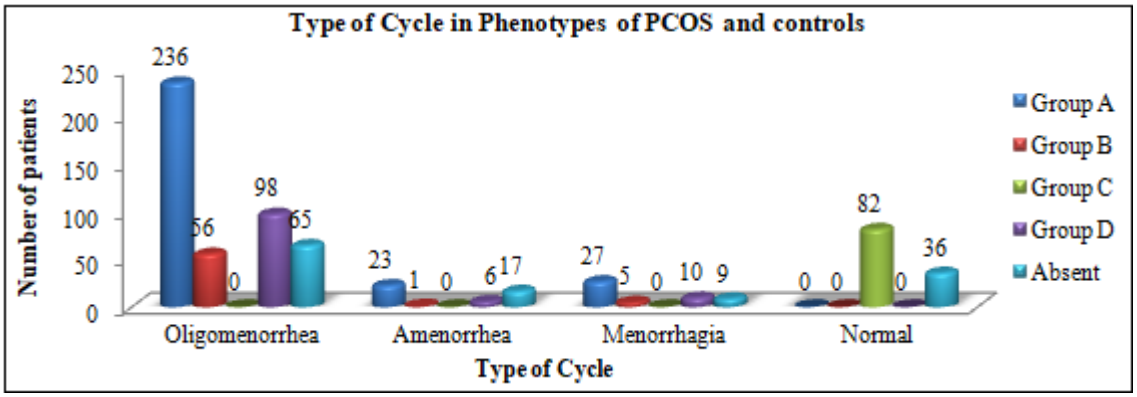

Figure 6: Bar diagram showing comparison of types of menstrual irregularities in PCOS phenotypes and controls

Table no 4 and Figure no 6 showed that group D patients had highest number of patients with oligomenorrhea while amenorrhea is common in group A patients and controls.

Table 5: Distribution of phenotypes of PCOS and Controls according to BMI

BMI	PCOS Phenotypes				Controls
	Group A	Group B	Group C	Group D	
< 18.50	13(4.6)	2(3.2)	1(1.2)	5(4.4)	13(10.3)
18.50 - 22.99	167(58.4)	41(66.2)	49(59.8)	70(61.4)	75(59)
23.0 to 29.99	87(30.4)	11(17.7)	27(32.9)	28(24.6)	39(30.7)
≥ 30	19(6.6)	8(12.9)	5(6.1)	11(9.6)	0
Total	286(100)	62(100)	82(100)	114(100)	127

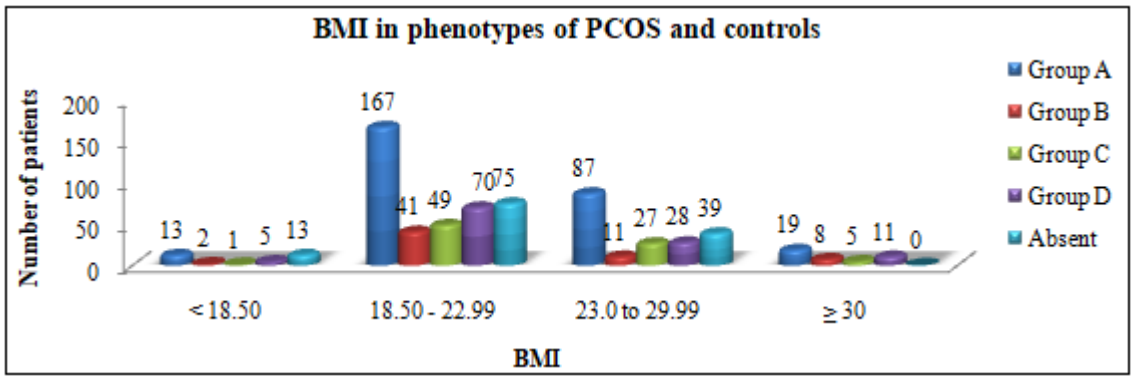

Figure 7: Frequency distribution of phenotypes of PCOS and controls according to BMI

Maximum overweight patients were found in group C followed by group D while maximum obese patients were found in group B where no control was obese.

Table 6: Distribution of PCOS phenotypes and controls according to WHR

WHR	PCOS phenotypes				Controls
	Group A	Group B	Group C	Group D	
Abnormal (> 0.85)	78(27.3)	17(27.4)	27(33)	31(27)	23(18)
Normal (≤ 0.85)	208(72.7)	45(72.6)	55(67)	83(73)	104(82)
Total	286(100)	62(100)	82(100)	114(100)	127(100)

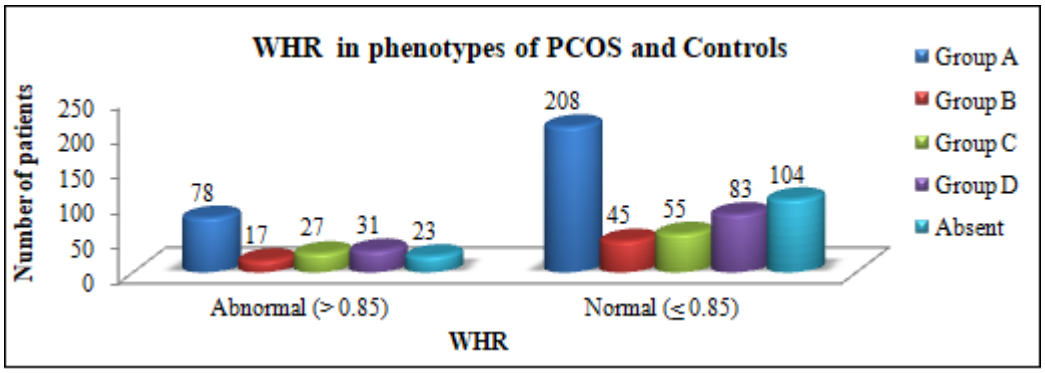

Figure 8: Frequency distribution PCOS phenotypes and controls according to WHR

Out of 544 PCOS patients 153(28.13%) patients had abnormal WHR which is statistically significant. Group C had highest number of patients with abnormal WHR (32.92%) followed by groups B (27.4%), A (27.3%) and D (27.1%)

Table 7: Distribution of all PCOS phenotypes and non PCOS patients according to HOMA-IR

HOMA IR	**PCOS phenotypes**				Controls (%)	Total (%)	p-value
	Group A(%)	Group B(%)	Group C(%)	Group D(%)			
Abnormal (> 3.5)	11(3.8)	6(9.6)	3(3.6)	3(2.6)	0	23(3.4)	0.010
Normal (≤ 3.5)	275(96.2)	56(90.4)	79(96.4)	111(97.4)	127(100)	648 (96.6)	
Total	286	62	82	114	127	671	

Significant (p-value < 0.05) Fisher's exact test used

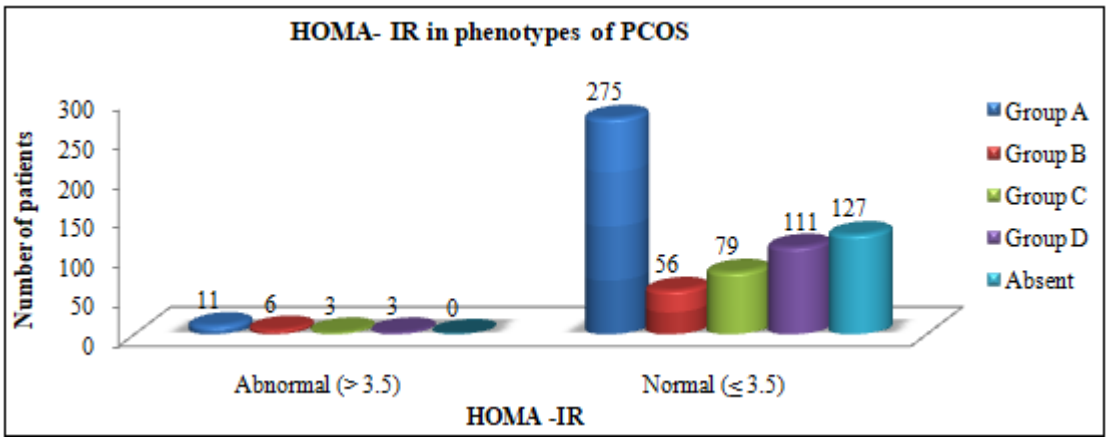

Figure 9: Frequency distribution of PCOS phenotypes and controls according to HOMA-IR

Out of 544 patients, 23 had HOMA-IR >3.5 than controls which is statistically significant.

Group B had maximum patients with raised HOMA-IR followed by groups A,C and least in group D and controls.

Out of 544 patients, 111 PCOS patients had abnormal LH/FSH ratio than controls which is highly significant. Group A(34%) had maximum number of patients with abnormal LH/FSH ratio.

Table 8: Distribution of PCOS phenotypes and controls according to abnormal serum testosterone

Testosterone	PCOS phenotypes				Controls (%)	Total (%)	p-value
	Group A (%)	Group B (%)	Group C (%)	Group D (%)			
Abnormal (> 0.68)	285(99.6)	59(95.2)	75(91.5)	44(38.6)	17(13.4)	480(71.5)	< 0.001
Normal (≤ 0.68)	1(0.4)	3(4.8)	7(8.5)	70(61.4)	110(86.6)	191(28.5)	
Total	286	62	82	114	127	671	

Significant (p-value < 0.05) Fisher's exact test used.

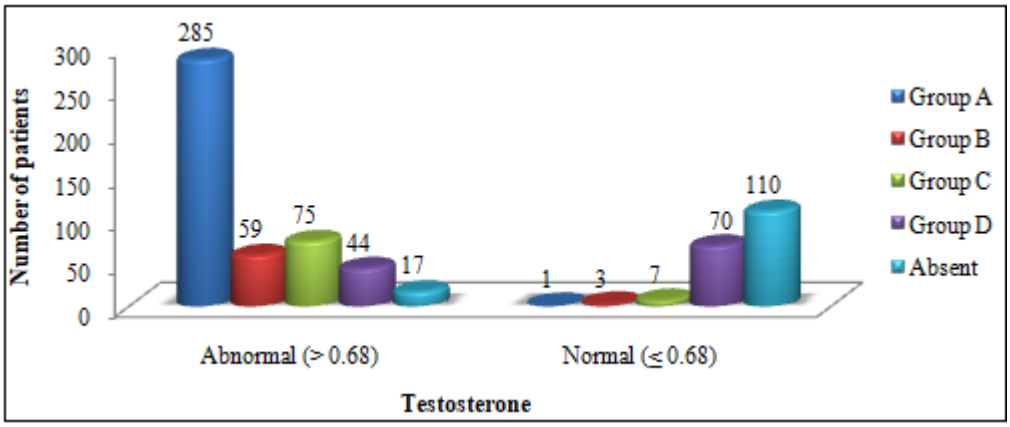

Figure 10: Frequency distribution of PCOS phenotypes and controls according to abnormal serum testosterone.

Out of 544 patients, 463 PCOS patients had abnormal serum testosterone than controls which is highly significant. Group A (99.6%) had maximum number of patients with serum testosterone >0.68 followed by groups B and C and least in group D and controls .

Table 9: Mean values of all parameters (mean±S.D)

Parameters	PCOS phenotypes				Controls 127	P –value
	Group A 286	Group B 62	Group C 82	Group D 114		
BMI	24.10±3.87	24.21±3.92	24.58±3.20	23.56±4.33	22.60±3.21	0.001
WC	82.27±8.29	82.14±6.13	83.79±5.34	81.52±6.93	79.79±9.53	0.005
WHR	0.80±0.073	0.80±0.065	0.82±0.054	0.80±0.076	0.78±0.064	0.01
F-G	7.511±.44	7.37±1.79	8.12±1.75	4.89±0.95	4.83±0.88	<0.001
FSH	5.91±1.51	6.10±0.79	6.82±1.74	5.77±1.63	5.62±1.50	<0.001
LH	10.70±2.96	9.12±2.82	9.70±2.20	7.30±2.49	4.61±1.70	<0.001
PRL	14.51±2.13	14.04±1.95	14.50±2.25	14.14±2.28	12.57±2.18	<0.001
TSH	2.12±1.80	2.46±3.50	1.85±0.67	2.16±0.75	1.83±0.73	0.09

FBG	92.24±8.83	89.60±10.44	87.67±8.50	86.75±10.38	78.53±6.97	<0.001
INSULIN	11.37±1.55	10.92±2.01	10.32±1.41	10.12±1.80	8.21±1.35	<0.001
HOMA-IR	2.60±0.53	2.44±0.66	2.25±0.50	2.19±0.58	1.59±0.34	<0.001
TESTOSTERONE	1.186± 0.195	1.082±0.323	1.100±0.274	0.628±0.142	0.509±0.146	<0.001

ANOVA test used ; $p<0.05$ is significant

5. Discussion

PCOS is a heterogeneous disorder and the Rotterdam criteria may have expanded the prevalence of this disease in the reproductive age female population by as much as 50% according to some estimates (1).

Phenotypic distribution

In our study, 671 women in reproductive age group (18-35 years) were recruited. Out of them, 544 had satisfied the criteria for PCOS, 127 women were found to be non-PCOS. They were divided into four standard phenotypical groups according to ESHRE/ASRM (2003) (11). Prevalence of women with PCOS was maximum for phenotype A (H+P+O; 52.57 %) followed by phenotype D (O+P; 20.97 %), phenotype C (H+P; 15.07 %) and phenotype B (H+O; 11.39 %). Similar results were found in study done by Sujatakar et al(12)on 410 women, they concluded that the largest group was PCOS Group A complete (H+P+O; 65.6%) followed by Group D (*P*+O; 22.2%); Group B (H+O; 11.2%) and Group C (*P*+H; 0.9%). These differences in prevalence of different phenotypes depends on the genetic, racial/ethnic and geographic variations. Phenotypes may also vary depending upon the study population from where patients have been recruited that is from infertility, gynecology, dermatology and endocrine clinics.

Table 10: Comparison of prevalence of PCOS phenotypes (12, 13, 14, 15, 16)

Author	Population	Group A (%)	Group B (%)	Group C (%)	Group D (%)
Our study	Pune (India)	52.57	11.40	15.07	20.96
SujataKar; 2013	Orissa (India)	65.6	11.2	0.9	22.2
HY Zhang; 2009	Chinese	26.8	7.6	13.4	52.2
SaxenaPikee; 2016	New Delhi (India)	20.85	11.37	31.28	12.80
SedaAtes; 2013	Turkish	47.1	13.2	21.2	18.5
OlgierdGluszak 2011	Poland	60.2	16.1	18.3	5.4

Clinical Features:

The most common symptom in our study was menstrual irregularity. 84.92% of PCOS patients had irregular menses, followed by weight gain in 60.29% and hirsutism in 56.04%

Menstrual irregularity

In adolescent and young women, the age of onset of obesity and that of menstrual irregularities are significantly co-related (17). Our study had observed that menstrual irregularities was present in 84.92% of PCOS patients; where as Majumdar and Singh have compared the clinical features of PCOS in Indian women. The authors have reported prevalence of menstrual irregularities as 79.2% vs. 44% in obese vs. non-obese women (18). Sunita J Ramanand et, had reported the prevalence of oligomenorrhea as 66.67% in obese and 60% in non-obese women (19).

BMI

The present study showed that high BMI was statistically significant in all PCOS phenotypes than controls and this result was similar to the study done by Pikee et al, H Y Zang et al, SedaAtes et al, which also showed significantly higher BMI in all phenotypes of PCOS (14,13,15). But in contrast to that, study done by Olgierd Gluszak et al, showed that there was no statistical significance between high BMI and different PCOS phenotypes (16).

Table 11: Comparison of BMI of PCOS phenotypes(in mean ±SD) (14,13,15,16).

Author	Group A	Group B	Group C	Group D	Control	P value
Our study	24.1±3.87	24.2±3.92	24.6±3.2	23.6±4.3	22.6±3.2	0.001
SaxenaPikee et al	26.2±5.43	28.1±6.01	25.7±5.66	24.49±5.09	21.35±2.51	<0.001
H Y Zang et al	36.5±8.6	35.8±9.3	30.9±8.3	28.6±6.5	27.3±5.2	<0.05
SedaAtes et al	27.26±7.05	25.96±6.11	25.88±5.49	25.03±5.97	24.09±4.47	0.001
OlgierdGluszak et al	26.22±7.1	28.95±7.2	26.12±6.5	28.38±8.6	-	>0.05

Our study showed that, groups A, B, C had higher BMI as compared to group D and controls; where group A had maximum overweight (45.3%) and obese women (44%); whereas Saxena Pikee et al, observed that overweight women were maximum in phenotype B (66.66%)(14).

Obesity is often associated with metabolic disorders, lean women with PCOS also have been found to have hyperinsulinemia and dyslpidemia (20).

This variance may be due to different criteria used for defining overweight and obese in different studies. It may also depend on the prevalence of obesity in that population.

Waist –Hip Ratio (WHR):

Our study observed that prevalence of WHR was significantly higher in all phenotypes than controls ($p=0.025$). Similar results were found by study done by Saxena Pikee et al in 2016 ($p<0.02$), SedaAtes et al in 2013 ($p=0.003$), SujataKar et al in 2013 ($p=0.001$)(14,15,12). In contrary to that study done by OlgierdGluszak et al in 2012,

showed no statistical significance between different phenotypes and WHR (16).

Table 12: Comparison of WHR of PCOS phenotypes (in mean ±SD)(15,14)

Author	Group A	Group B	Group C	Group D	control	P value
Our study	0.808±0.073	0.809±0.065	0.826±0.054	0.8±0.076	0.787±0.064	0.025
SedaAtes et al	0.83±0.08	0.83±0.07	0.82±0.07	0.82±0.08	0.8±0.08	0.003
SaxenaPikee et al	0.814±0.88	0.802±0.086	0.78±0.121	0.814±0.093	0.75±0.068	0.02

P<0.05, significant; P<0.001, highly significant

Study performed by Kavita Mandrelle et al in vellore in 2012, concluded that infertile women with PCOS, particularly those with age ≥25 years or with central obesity (a waist hip ratio of ≥0.85), are at a higher risk of developing metabolic syndrome and should be offered screening tests(21).

Predictors of Insulin Resistance

Acanthosisnigricans

Acanthosisnigricans, when not related to malignancy, is considered to be a dermal manifestation of hyperinsulinaemia (22, 23, 24). Women with acanthosisnigricans and obesity represent the severest form of the polycystic ovary syndrome (25).

In our study, acanthosisnigricans (AN) was described in 27.94% of all the PCOS women, while study done by Sujatakar et al in 2013 showed that, it was detected in 37.5% of all PCOS women (12). In contrast to the study done by Himabindu Sangabathula et al in 2017, showed only 16 % women with it (26) .

Glucose

Our study results found that serum fasting blood glucose level was significantly higher in all the PCOS patients, this results were supported by SaxenaPikee et al study (14). According to our study, phenotype A had highest women (18.53%) with abnormal fasting glucose (> 100 mg/dl) while least was in group D (8.7%) and controls (0%).

Table 13: Phenotypic distribution of serum FBG (mg/dl) of different phenotypes of PCOS (mean±S.D.)

Author	Group A	Group B	Group C	Group D	P value
Our study	92.24±8.83	89.60±10.44	87.67±8.5	86.75±10.38	< 0.001
SaxenaPikee et al study in 2013	90.65±18.27	70±30.62	99.25±21.95	86.78±22.26	-
HY Zang et al study in 2009	93±12	96±25	96±30	89±10	-
OlgierdGluszak et al,Study in 2012	87.68±11.94	82.37±10.45	84.40±8.93	80.00±7.07	-
SujataKar et al study in 2013	95.25±12.24	90.18±8.39	94.55±15.8	92±13	0.090

p<0.05, significant; p<0.001,highly significant

Above table showed, all mean values are comparable.

Insulin

Polycystic ovary syndrome (PCOS) is not only a reproductive endocrinopathy but also a metabolic disorder. PCOS is associated with hyperinsulinemia, glucose intolerance, obesity and altered lipid profile (27, 28). In our study the mean serum fasting insulin levels in all the groups of PCOS was significantly higher to control group (p<0.001). Similar results were found in the study done by SaxenaPikee et al (14).

Table 14: Phenotypic distribution of serum fasting insulin (mIU/L) of different phenotypes of PCOS (14,13,16,12) (mean ±SD)

Author	Group A	Group B	Group C	Group D	P value
Our study	11.37±1.55	10.92±2.01	10.32±1.41	10.12±1.8	<0.001
Saxena Pikee et al study in 2013	19.08±19.26	26.82±22.32	13.47±15.11	15.8±26.47	<0.001
HY Zang et al study in 2009	17.1±13.8	17.2±13.6	16.3±12.8	12.9±10.3	<0.05
Olgierd Gluszak et al, Study in 2012	7.67±5.49	9.71±4.39	8.25±3.33	8.50±6.36	-
Sujata Kar et al study in 2013	14.14±9.8	10.32±7.48	16.85±14.05	2.52	0.05

p<0.05, significant; p<0.001, highly significant

Our study showed that, serum fasting insulin was highly significant with PCOS and levels are higher in hyperandrogenic phenotypes like group A, group B and group C. This was supported by H Y Zang et al in 2009 (13), while studies done by SaxenaPikee et al and Olgierd Gluszak et al observed that group B had highest serum fasting glucose(14,16). Insulin sensitivity was found to be normal in muscle, liver, and adipose tissue in slim women with PCOS (29).

Homeostasis model assessment for IR (HOMA-IR)

IR was estimated using the HOMA-IR (fasting insulin μU/mL × fasting glucose (mg/dl)/22.5) (16). In our study, IR was calculated with a HOMA-IR, where it's cut off value was taken as ≥3.5 (12).

Table 15: Phenotypic distribution of different phenotypes HOMA-IR of PCOS (13,16,12) (mean±S.D.)

Author	Group A	Group B	Group C	Group D	Control	P value
Our study	2.6±0.53	2.44±0.66	2.25±0.50	2.19±0.58	1.59±0.34	<0.001
HY Zang et al study in 2009	5.86±3.23	5.76±6.6	4.63±5.19	3.65±2.97	3.24±3.5	<0.05
OlgierdGluszak et al,Study in 2012	1.77±1.49	2.04±0.93	1.78±0.80	1.73±1.40	-	>0.05
SujataKar et al study in 2013	3.43±2.71	2.9±2.2	4.19±3.05	2.52±0.5	-	0.17

p<0.05,significant ; p<0.001,highly significant

Above table showed HOMA-IR is highly significant in all phenotypes of PCOS. Study conducted by HY Zang et al in 2009 also had similar results showing HOMA-IR which was significant in all PCOS phenotypes (13).

Our study found that, insulin resistance (HOMA-IR) is highest in group B (9.68%) followed by group A (3.85%), group C (3.66%) and least in group D (2.63%) and controls (0%); similarly study done by SujataKar et al study in 2013 showed that group B (35.13%) had highest prevalence of insulin resistance followed by group A (31.58%) and group D (21.05%) (30).

Insulin resistance is thought to be the important pathogenic factor in the development of hypertension, glucose intolerance, obesity, lipid abnormalities and coronary artery disease, which together constitutes the metabolic syndrome (31). Studies done on Indian population, though limited, have suggested that abnormalities of the insulin receptors are more common in Indian women with PCOS compared to white women with PCOS (32).

Sujatha et al opined that insulin resistance and compensatory hyperinsulinemia are associated with atherogenic lipid profile, high blood pressure and increased risk of developing type 2 diabetes mellitus .This clustering of haemodyamic and metabolic abnormalities is associated with a significant increase in risk of coronary heart disease, cerebrovascular disease and peripheral vascular disease (33).

Sujatha et al (33) further recommends treatment of insulin resistance which will reduce ovarian androgen secretion and can cause resumption of ovulatory menstrual cycle. It also improves the clinical and biochemical features of PCOS and decreases the risk of endometrial and breast malignancies, cardiovascular and cerebrovascular disease. This also corresponds with studies by GadirA et al and Soloman CG et al (34, 35).

Serum total Testosterone

Table 16: Phenotypic distribution of serum total testosterone (ng/ml) of different phenotypes of PCOS (15,16,14) (mean±S.D.)

Author	Group A	Group B	Group C	Group D	Control	P value
Our study	1.186±0.195	1.082±0.325	1.1±0.274	0.6±0.142	0.5±0.146	<0.001
SedaAtes et al study in 2013	0.68±0.53	0.53±0.25	0.54±0.24	0.41±0.14	0.36±0.14	<0.001
OlgierdGluszak et al,Study in 2012	0.88±0.31	0.78±0.15	0.76±0.3	0.55±0.1	-	<0.04
SaxenaPikee et al study in 2013	33.27±35.75	35.69±25.55	22.56±29.11	2.12±3.65	0.58±0.49	<0.001

p<0.05, significant ; p<0.001,highly significant

In our study, mean free testosterone level were significantly higher (P<0.001) in all phenotypes of PCOS as compared to controls. Similar results were found in the study done by OlgierdGluszak et al (P<0.04), SaxenaPikee et al (P<0.001) and SedaAtes et al study (P<0.001) (16,14,15). Sujatha et al opined in their study that there is a cause and effect relationship between insulin resistance, hyperandrogenism and an ovulation (33).

Components of metabolic syndrome

Waist circumference (WC)

In our study, waist circumference was abnormal (>88cm) in 27.76% of all the PCOS patients, which is significantly higher (P<0.05) than controls and highly associated with risk of having metabolic syndrome. Similar results were observed in study conducted by SujataKar et al in 2013 (12), where they found that WC (≥80cm) was highly significant (p=0.001) in all the PCOS patients.

Table 17: Comparison of Odd's ratio for WC(>88 CM) (12).

WC(cut off in cm)	Author	OR	CI
>88	Our study	2.29	(1.44 – 4.28)
≥80	SujataKar et al	3.68	1.6807-8.0737(95%)

OR -Odds Ratio; CI-Confidence Interval

BP

In our study, BP was abnormal (>130/80 mmhg) in 9.93 % of all the PCOS patients, which is significantly higher (P<0.05) than controls and highly associated with the risk of having metabolic syndrome [Odds ratio (C.I) is 13.89 (1.90 – 101.35)]. Similar results were observed in the study conducted by SaxenaPikee et al (14), they found that diastolic BP was significantly higher in all the phenotypes of PCOS with reference to controls (p<0.013).Thus various phenotypes of PCOS manifest clinical, metabolic and endocrine differences. These observations may influence future management protocols like lifestyle modification to delay the onset and effects of metabolic syndrome and management of infertility. Although obesity is often associated with metabolic disorders, lean women with PCOS also have hyperinsulinemia which is one of the risk factors for cardiovascular diseases.

General prevalence of insulin resistance in South Asian women with PCOS is quite high. More research is needed to find out the reason for insulin resistance and dyslipidemia in Indian population.

6. Conclusion

PCOS is a common complex endocrine condition in women associated with psychological, reproductive and metabolic features. It is a chronic disease with manifestations across the lifespan and represents a major health and economic burden. Hyperandrogenic PCOS patients (group A, B, C) are associated with more deranged endocrine and metabolic profile than non hyperandrogenic PCOS (group D). It is important therefore that clinicians caring for patients with hyperandrogeic PCOS understand not only management issues pertinent to their speciality but also appreciate the other potential health risks in these women and counsel accordingly.

7. Recommendations

- There are many studies on PCOS focused on specific factors but further study which is more comprehensive, population based and includes all parameters is recommended.
- As phenotypic distribution is already done, longitudinal long term follow up study of these women to evaluate effects on future fertility and onset of metabolic disorders and risk of endometrial carcinoma is therefore recommended.
- Childhood obesity is rapidly increasing and as lifestyle modifications is the only preventive measure available, screening of younger adolescent group can help to reduce incidence of disease.

8. Limitations

- Our study was single hospital based and not community based so actual distribution of PCOS phenotypes in population may differ slightly.
- All biochemical investigations of patient like lipid profile, serum DHEA-S could not be possible due to cost constraint.
- Long term follow up of those patients was not done.

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