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Prevalence And Phenotypic Spectrum of Polycystic Ovarian Syndrome and Associated Metabolic Risks in a Rural North Indian Tertiary Care Setting

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KEYWORDS

Body mass index, Obese, Metabolic syndrome, Diabetes mellitus, Polycystic ovarian syndrome, Phenotype.

ABSTRACT:

Background and Objectives: Polycystic ovarian syndrome (PCOS) is a multisystem, non-communicable disease of growing concern among women and is most common endocrinopathy among women of reproductive age. The ovaries of women with this syndrome are polycystic and conform to a specific anatomical appearance that may be detected on ultrasound imaging, although the ovarian morphology can exist in women without the overt clinical manifestations.

Primary Objective:

The aim of study is to determine the prevalence of PCOS among women of reproductive age attending gynaecology OPD in a tertiary care hospital in rural area of North India.

Secondary Objectives:

To study the clinical subtypes of PCOS among women with PCOS attending gynaecology OPD.

To study the presenting complaints; clinical characteristics, anthropology and USG features of the patients diagnosed with PCOS.

To study clinical profile of patient and co-morbidities associated with polycystic ovarian syndrome.

MATERIAL & METHODS

This hospital based observational study was conducted at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana where five hundred and four women in reproductive age group were screened which included both adolescents and adults attending Gynaecology out-patient clinic. The women with menstrual irregularity (oligomenorrhea/amenorrhea) or infertility with or without clinical evidence of hyperandrogenism who were diagnosed as having polycystic ovarian syndrome according to Rotterdam's criteria were included in the study.

CONCLUSION: The prevalence of PCOS in our study was 14% with phenotype A being the most prevalent phenotype. Menstrual dysfunction was the most common presenting complaint with hirsutism, acne and infertility being the other common presentations. Majority of patients with PCOS were found to be obese however, 37.14% lean PCOS patients were also seen.

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Introduction

Polycystic ovarian syndrome (PCOS) is a multisystem, non-communicable disease of growing concern among women and is most common endocrinopathy among women of reproductive age. The ovaries of women with this syndrome are polycystic and conform to a specific anatomical appearance that may be detected on ultrasound imaging, although the ovarian morphology can exist in women without the overt clinical manifestations.[1]The main clinical manifestations of PCOS are hyperandrogenism and irregular menstruation, the latter of which leads to infertility. The associated metabolic dysfunction includes insulin resistance, dyslipidemia and increasing prevalence of obesity. The underlying mechanism(s) of PCOS are responsible for the abnormalities of hypothalamic-pituitary ovarian-adrenal function and altered metabolic physiology. All of these factors may contribute to the clinical phenotype and pose increased long-term health risks.[2,3]

Thus, PCOS can be described as a multisystem reproductive-metabolic disorder with clinical manifestations like hyperandrogenism (hirsutism and acne) and oligo-anovulation (oligomenorrhea, infertility, and dysfunctional uterine bleeding) with radiological findings of polycystic ovaries excluding other endocrinopathies.[4] The National Institutes of Health (NIH)-sponsored conference 1990 defined PCOS as hyperandrogenism and/or hyperandrogenemia with oligo-anovulation, (excluding other endocrinopathies e.g., congenital adrenal hyperplasia (CAH), Cushing syndrome, thyroid dysfunction, hyperprolactinemia, androgen- producing tumors, and drug-induced androgen excess). The Rotterdam consensus modified the diagnostic criteria in 2003 and was revised in 2004[3] by the European Society for Human Reproduction Medicine (ESHRE) in collaboration with the American Society for Reproductive Medicine (ASRM) to include at least two of the following three features: (1) clinical or biochemical hyperandrogenism, (2) oligo-anovulation, and (3) polycystic ovaries, excluding the previously described endocrinopathies. These newer Rotterdam criteria for PCOS are currently recommended for clinical use and include all patients defined by 1990 NIH criteria (i.e., classic PCOS) along with women with either (1) clinical/ biochemical hyperandrogenism and polycystic ovaries (i.e., ovulatory PCOS) or (2) polycystic ovaries with ovulatory dysfunction. The use of broader Rotterdam criteria has almost doubled the prevalence of PCOS from 6-10 % to 21% of women.[4] Depending on the PCOS definition used, different phenotypes of the PCOS exist. The division into phenotypes is based on the characteristics of PCOS with oligo/amenorrhea, hyperandrogenism and PCO (Polycystic ovaries). The knowledge of the specific phenotypes of a study population is important, as exemplified by the knowledge that there is an increased risk of metabolic dysfunction in women whose phenotype includes hyperandrogenism, however most studies have not reported such an increased risk in women with PCO, with or without oligo/anovulation.[5] PCOS is a complex disorder where numerous genetic and environmental factors act and contribute to its pathophysiology. It has been observed that the likelihood of PCOS in sisters and mothers of affected women is considerably higher than general population indicating familial occurrence. Several factors may be involved in its development. PCOS disease exists as a genetic predisposition in the person and its symptoms are exacerbated by environmental factors and lifestyle.[2] The genes which play an important role in PCOS are DENND1A gene, THADA gene, INSR and TOX3. Some studies show PCOS susceptibility variants in THADA and INSR are associated with metabolic syndrome and variants in TOX3 and DENNDIA are associated with insulin resistance.[6]However, only the association of a few genetic variants and mutations have been replicated in different population of patients with PCOS. PCOS is now considered a complex multigenic disorder with predisposing and protective genetic variants interacting with strong environmental influences to result in the different PCOS phenotypes. The transmission over generations of these variants may be the result of the survival advantage provided by them.[7] PCOS is a common cause of infertility in women of reproductive age group.[4] PCOS is not a disease exclusive to fertility and adolescent period but it can have implications in later life also. The presentation of disease in adolescent period may be in the form of amenorrhea, oligomenorrhea, hirsutism, obesity, and acne. In reproductive period, the patient may present with infertility and delayed menstrual cycles. In later age, PCOS can increase the risk of type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease and even endometrial cancer and possibly breast cancer in later life.[7]

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OBJECTIVES

Primary Objective

The aim of study is to determine the prevalence of PCOS among women of reproductive age attending gynaecology OPD in a tertiary care hospital in rural area of North India.

Secondary Objectives

To study the clinical subtypes of PCOS among women with PCOS attending gynaecology OPD.

To study the presenting complaints; clinical characteristics, anthropology and USG features of the patients diagnosed with PCOS.

To study clinical profile of patient and co-morbidities associated with polycystic ovarian syndrome.

MATERIALS AND METHODS

This hospital based observational study was conducted at Maharishi Markandeshwar Institute of Health Sciences And research (MMIMSR) Mullana, Ambala, Haryana, India. Women of reproductive age group (14-49) attending Gynaecology OPD were screened for polycystic ovarian syndrome for a period of 18 months.

METHODOLOGY

Five hundred and four women in reproductive age group, both adolescents and adults, attending Gynaecology out-patient clinic in the Department of Obstetrics and Gynaecology, Maharishi Markandeshwar Institute of Health Sciences and Research, Mullana, Ambala, Haryana, India. The women with menstrual irregularity (oligomenorrhea/amenorrhea) or infertility with or without clinical evidence of hyperandrogenism who were diagnosed as having polycystic ovarian syndrome according to Rotterdam's criteria were included in the study, after explaining the nature of the study and obtaining informed consent for participating in the study.Study duration is Eighteen Months.

Inclusion Criteria

All patients of reproductive age group (14-49) attending Gynaecology OPD.

Exclusion Criteria

Women with any other etiology for Hyperandrogenism or menstrualdisturbance than PCOS.

Pregnant women.

Patients not willing to participate in study.

Systematic sampling technique were employed for the study.

SOURCE OF DATA

Women of reproductive age group (14-49) attending Gynaecology OPD at, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala were enrolled in the study.

COLLECTION OF DATA

A total of 504 patients attending Gynaecology out-patient clinic were screened. Pre-designed pre-structured questionnaire comprising variables like age, education, occupation, marital history and family history were recorded.

History of dietary pattern, physical activity was recorded. BMI(Kg/m^2) was recorded by computing height and weight. Waist circumference and Waist hip ratio were noted. Blood investigations such a Fasting blood glucose, lipid profile, serum testosterone, serum TSH levels, Serum LH and FSH levels. Where indicated further tests were done to exclude other causes of menstrual irregularities and hyperandrogenism.

Ultrasound pelvis were done and observations were noted. Diagnosis of PCOS was according to Rotterdam criteria.

RESULTS

TABLE 1: TABLE SHOWING PREVALENCE OF PCOS AMONG WOMEN OF REPRODUCTIVE AGE GROUP PRESENTING TO GYNAE OPD (N=504)

TOTAL NUMBER OF PATIENTS	FREQUENCY	PERCENTAGE (%)
PCOS	70	14

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NO PCOS	434	86
TOTAL	504	100.0

Table 1 shows the prevalence of PCOS among women visiting in gynae OPD and found that out of the total 504 samples, 70 (14 %) women were having PCOS whereas the rest do not.

TABLE 2 (A): AGE DISTRIBUTION AMONG WOMEN OF REPRODUCTIVE AGE GROUP PRESENTING TO GYNAE OPD

Group	N	Mean	SD	Std. Error Mean
PCOS	70	28.81	3.95	0.47
NO PCOS	434	27.12	4.91	0.24

Table 2(a) shows the mean age of patients as 28.81± 3.95 years with range between 18 to 38 years.

TABLE 2(B): AGE DISTRIBUTION AMONG WOMEN OF REPRODUCTIVE AGE GROUP PRESENTING TO GYNAE OPD AND OF WOMEN WITH PCOS AMONG THEM.

AGE (In Years)		**PCOS**		**TOTAL(n=504)**
		NO (n=434)	YES (n=70)	
<20	N	30	5	35
	%	6.9%	7.14%	6.9%
21-25	N	118	2	120
	%	27.2%	2.9%	23.8%
26-30	N	182	43	225
	%	41.9%	61.4%	44.6%
31-35	N	80	19	99
	%	18.4%	27.1%	19.6%
>35	N	24	1	25
	%	5.5%	1.43%	5%

Table 2 (b) shows the age distribution of the women who visit gynae OPD for different concerns related to their health and found that majority of the cases with PCOS (61.4%) belonged to the age group 26-30 years whereas only 20 cases (28.5%) were more than 30 years of age.

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TABLE 3: DISTRIBUTION OF PATIENTS WITH PCOS AS PER SOCIOECONOMIC CLASS (KUPPUSWAMY SCALE)

SOCIOECONOMIC STATUS	FREQUENCY	PERCENTAGE (%)
UPPER MIDDLE	20	28.6
LOWER MIDDLE	22	31.4
UPPER LOWER	23	32.9
LOWER	5	7.1
TOTAL	70	100.0

The socio-economic status of the patients was analyzed according to Modified Kuppuswamy Socioeconomic scale. Among PCOS patients, only 7.1% cases were from lower socioeconomic class and rest of the cases were distributed almost equally among Upper Middle (28.6%), Lower Middle (31.4%) and Upper Lower socioeconomic class (32.9%).

TABLE 4: DISTRIBUTION OF PCOS PATIENTS AS PER PHENOTYPE OF PCOS

	PHENOTYPE	FREQUENCY	PERCENTAGE (%)
	PHENOTYPE A	39	55.7
	PHENOTYPE B	10	14.3
	PHENOTYPE C	13	18.6
	PHENOTYPE D	8	11.4
	TOTAL	70	100.0

Phenotype A: AE+OD+PCOM, Phenotype B: AE+OD, Phenotype C:AE+PCOM, Phenotype D: OD+PCOM(AE: Androgen excess; OD: Ovulatory dysfunction; PCOM: Polycystic ovarian morphology

Table 4 shows Distribution of patients as per phenotype of PCOS, majority of patients (55.7%) had phenotype A, 14.3% patients had phenotype B, 18.6% patients had phenotype C and 11.4% patients had phenotype D.

TABLE 5: DISTRIBUTION OF PATIENTS WITH PCOS AS PER MARITAL STATUS

MARITAL STATUS	FREQUENCY	PERCENTAGE (%)
MARRIED	46	65.7
UNMARRIED	24	34.3
Total	70	100.0

In present study, 34.3% patients with PCOS were unmarried whereas 65.7% patients were married.

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TABLE 6: ASSOCIATION OF AGE OF WOMEN WITH PCOS WITH PHENOTYPE OF PCOS

PHENOTYPE		Class				Total
		Class A	Class B	Class C	Class D	
age group	15-20	3(7.7%)	1(10%)	0	1(12.5%)	5(7.1%)
	21-25	1(2.6%)	1(10%)	0	0	2(2.9%)
	26-30	21(53.8%)	5(50%)	11(84.6%)	6(75%)	43(61.4%)
	31-35	14(35.9%)	2(20%)	2(15.4%)	1(12.5%)	19(27.1%)
	>35	0	1(10%)	0	0	1(1.5%)
Total		39	10	13	8	70
Chi-square value- 14.32, p value- 0.28, non-significant						

Majority of the patients were in the age group 26-35 years of age with Phenotype A being the most common. However, the difference between different age group was not significant (p value- 0.28)

TABLE 7: ASSOCIATION OF LOW HDL WITH PHENOTYPE OF PCOS

PHENOTYPE		Class				Total
		Class A	Class B	Class C	Class D	
HD L	LOW HDL	6 (15.4%)	2 (20%)	0	0	8
	NORMAL	33	8	13	8	62
Total		39	10	13	8	70

In above table, 20 % of patients in class B and 15.4% in class A had low HDL.

The cases with high cholesterol levels and high triglyceride levels were assessed for their phenotypes and no significant difference was observed between the 4 phenotypes and cholesterol and triglyceride in present study. In class B, 20% of cases had low HDL and 15.4% cases in class A had low HDL. However, on statistical evaluation, these differences were not significant.

DISCUSSION

Polycystic ovarian syndrome is a multisystem disorder that effects multiple aspects of women overall health and has long term health implications. In young adolescents it may be responsible for acne, hirsutism, obesity which can create a negative body image. Delayed cycles and subfertility related to PCOS may affect adversely the quality of life of women of reproductive age group. Long term effects such as metabolic syndrome, type 2 diabetes mellitus, obstructive sleep apnea can add to the cardiovascular morbidity in later age. Due to rising incidence of obesity and environmental factors and better diagnostic facilities an increase in women diagnosed with PCOS has been observed over the last few decades. The prevalence of PCOS also depends on the environmental factors and genetic factors and great variations have been observed in different geographical areas. In India, variations in prevalence of PCOS have been observed in different studies belonging to different states.

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TABLE 8: PREVALENCE OF PCOS IN VARIOUS STUDIES

Author, year	Region	Age group(years)	Criteria to diagnose PCOS	Sample size	Prevalence (%)
Nidhi et al[8] (2011)	Andhra Pradesh	15-18	Rotterdam's, NIH	460	9.13%(Rotterdam's), 2.6% (NIH)
Vijaya K et al[9] (2014)	Pondicherry	19-25	Rotterdam's	238	11.7%(Rotterdam's)
Bhuvanashree et al[10] (2013)	Andhra Pradesh	10-19	Rotterdam's	253	15.4%(Rotterdam's)
Joshi B et al[11] (2014)	Mumbai (Maharashtra)	15-24	Rotterdam's, AE-PCOS)	600	22.5% (Rotterdam's), 10.6% (AE-PCOS)
Deswal R et al[12] (2014)	Rohtak (Haryana)	16-45	Rotterdam's	325	6.8% (Rotterdam's)
Choudhary A et al[13] (2017)	Uttarakhand, UP	16-30+ (reproductive age group)	NIH	170	41% (NIH)
Ganie MA et al[14] (2017)	Kashmir	15-40	Rotterdam's, NIH, AES	964	35.3% (Rotterdam's), 28.9% (NIH),
Gupta et al[15] (2018)	Madhya Pradesh	17-24	Rotterdam's	500	8.2% (Rotterdam's)
Nanjaiah R et al[16] (2018)	Karnataka	18-30	Rotterdam's	396	4.5% (Rotterdam's)
Laddad et al[17] (2019)	Maharashtra	10-19	Rotterdam's	150	17.3% (Rotterdam's)
Mehreen TS et al[18] (2021)	Chennai	12-30	Rotterdam's, NIH, AE- PCOS	518	8.1%(Rotterdam's), 2.1% (NIH), 2.9% (AE-PCOS)

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Present study (2022)	Haryana	14-49	Rotterdam's	504	14%

In the present study, the prevalence of PCOS in women presenting to outpatient department in a rural tertiary care Health center in Haryana was found to be 14% using Rotterdam's criteria. Similar studies have been done in different areas of different states in India and among different age groups of women.Vijaya K et al[9] (2014) from Pondicherry reported prevalence of PCOS as 11.6%. by Rotterdam's criteria in young women. In a study from Andhra Pradesh, conducted by Nidhi R et al[8], the prevalence rate was 9.13% among young adults. Joshi B et al (2014) reported prevalence of PCOS from Mumbai to be 22.5 %.**Ganie M et al**[14] (2017) in a cross-sectional study from Kashmir observed the prevalence to be 35.3 % in women of reproductive age group using Rotterdam criteria which was higher than our study. Choudhary A et al (2017) in their study on women of reproduction age group found the prevalence of PCOS as 40% in a tertiary care institute in Uttarakhand (Uttar Pradesh). Gupta M et al (2018) from Madhya Pradesh, Nanjaiah R et al[16] (2018) from Karnataka, Mehreen TS et al[18] from Chennai reported prevalence of PCOS as 8.2%, 4.5%, and 8.1% respectively which were much lower when compared to our study.

TABLE 9: PREVALENCE OF PCOS IN VARIOUS INTERNATIONAL STUDIES

Author, year	Region	Age group(years)	Criteria to diagnose PCOS	Sample size	Prevalence (%)
Gabrielli L et al (2012)	Brazil	18-45	Rotterdam's	859	8.5%
Li R et al (2013)	Beijing, China	19-45	Rotterdam's	15,924	5.6%
Kumarapeli V et al (2008)	Sri Lanka	15-39	Rotterdam's	3030	6.3%
Pembe AM et al (2009)	Tanzania	18-45	Rotterdam's	100	32%
March WA et al (2010)	Australia	27-34	Rotterdam's	728	11.9%
Fatima K et al (2021)	Dhaka (Bangladesh)	15-35	Rotterdam's	100	6.11%

Family History of PCOS

In the present study, 40% had family history of PCOS. When family history of PCOS was taken it was observed in the study by Singh A et al (2018) that about 43% had positive family history in first degree relative. In the study done by Kahsar MD et al of the 78 mothers and 50 sisters evaluated clinically, 19 (24%) and 16 (32%) were affected with PCOS. Authors concluded that there is genetic predisposition for PCOS. In the study by Nanjaiah R et al (2018) 3.8% had family history of PCOS.

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PHENOTYPE OF PCOS

The presentation of PCOS is subdivided into 4 Phenotypes: Phenotype A: HA+OD+PCOM, Phenotype B: HA+OD, Phenotype C: HA+PCOM and Phenotype D: OD+PCOM (Rotterdam's criteria)Phenotype A and B collectively are also termed under "Classic PCOS which is associated with more pronounced menstrual dysfunction, increased insulin levels, increased insulin resistance, increased BMI, prevalence of obesity and risk for metabolic syndrome.[4]In present study, Irregular cycles were the most common presenting complaint (61.42%) followed by excessive hair growth (54.28%). Other presenting complaints included acne (47.14%) and excessive weight gain (7.14%).Among married women, Infertility was second most common presenting complaint.

Menstrual Irregularities and hyperandrogenism

Menstrual dysfunction in PCOS is characterized by irregular, infrequent or absent menstrual bleeding. Most of the symptoms are due to Oligo/Anovulation whereas approximately 10% of women exhibit regular ovulatory cycles.In present study, irregular cycles were the most common presenting complaint (61.4%) in women with PCOS.

It was also the leading cause of seeking gynecological consult in married (60.8%) as well as unmarried women (62.5%) with PCOS.Excessive hair growth (Hirsutism) was the second most common presenting complaint (54.28%) in women with PCOS. Acne was reported by 47.14% of study population. Metabolic syndrome Metabolic syndrome is a constellation of metabolic disturbances which include central obesity, insulin resistance and hyperglycemia, dyslipidemia and hypertension.Metabolic syndrome was observed in 15.7% women with PCOS in our study. Deswal R et al[12] **(2020)**, in their systematic review reported metabolic syndrome in 6.01% women with PCOS (when Rotterdam's criteria were used for diagnosis of PCOS). South Asians have increased propensity to develop Metabolic syndrome due to increased waist hip ratio, waist circumference, increased insulin resistance and increased atherogenic dyslipidemia. Kaur J et al[19] (2019) reported Metabolic syndrome in 37% of women with PCOS in their study. They observed that metabolic syndrome was most prevalent in phenotype A (43%), followed by Phenotype B (39%), Phenotype C (31%) and phenotype D (28%). Authors concluded that metabolic syndrome appeared to be more common in hyperandrogenic phenotypes i.e., 85% (in A, B &C) than in non-hyperandrogenic phenotype D i.e., 15%.

Conclusion

PCOS is a sedentary life and obesity related disorder. The prevalence of PCOS has been increasing over last few decades primarily due to life style changes. PCOS has long term implications on women's health due to its increased propensity to chronic health diseases such as Diabetes, Hypertension, Obesity and Metabolic syndrome. Prevalence of PCOS among women presenting to our Rural Tertiary health care Hospital in Haryana was 14% with phenotype A being the most prevalent phenotype. Menstrual dysfunction is the most common problem of PCOS for which women seek healthcare guidance. Other common causes for seeking consultation are Hirsutism, Acne and Infertility. These can put a tremendous burden on women's physical and mental health if left untreated.

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