

ORIGINAL ARTICLE

Frequency and Relationship of Polycystic Ovarian Syndrome with Hirsutism

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ABSTRACT

Objectives: To estimate the frequency and relation of polycystic ovarian syndrome (PCOS) with hirsutism in normal and hirsute females.

Study Design: Cross-sectional analytical study.

Place and Duration: Department of Dermatology, Radiology and Immunoassay Laboratory at NHRC, Sheikh Zayed Medical Complex, Lahore from Dec 2008 – Dec 2009.

Patients and Methods: Clinically confirmed 50 hirsutes and 50 normal females aged between 14-20 years were included in the study while those with virilism, post menopausal, menopause cushing syndrome were excluded. Informed consent was obtained from eligible participants and demographic information was recorded in a study proforma. Ultrasound was done for polycystic ovaries (PCO) and adrenal hyperplasia. PCOS was further confirmed in accordance with revised Rotterdam definitions 2003 and its criteria. A modified Ferriman-Gallwey (FG) score was used to determine the severity of hirsutism. Five milliliters of fasting blood was drawn, serum separated and stored at -20°C, for analysis of luteinizing hormone and follicular stimulating hormone ratio (LH: FSH), free testosterone, dihydrotestosterone (DHT), cortisol and alanine transferase (ALT).

Results: A total 100 young females were studied. Most of the hirsute females (80%) had moderate to severe hirsutism. PCO was confirmed in 68% hirsute and 32% normal age matched group. Oligomenorrhea was present in 44% hirsute female and 4% normals. No direct association was seen among obesity, hirsutism and PCO. Disturbance of LH:FSH ratio was seen in all hirsute females with PCO while LH:FSH ratio was found normal in all PCO negative hirsutes and control females. Mean levels of free testosterone, DHT, cortisol and ALT were normal in both groups. **Conclusion:** About 68% hirsute and 32% normal females had PCO. The chances of having hirsutism in adolescents suffering from PCO alongwith oligomenorrhea is higher than that of in females with PCO alone.

Key Words: Hirsutism, Polycystic Ovarian Syndrome, Hormone Levels, BMI, Oligomenorrhea.

INTRODUCTION

Polycystic ovary syndrome is one of the most common endocrine disorders, affecting about 5-15% of women of reproductive age.^{1,2} Its aetiology is unknown³. However PCOS indicates multiple potential aetiologies and multivariate clinical presentations⁴. The condition is characterized by oligo-ovulation or anovulation, biochemical or clinical hyperandrogenism, and PCO. The cause of PCOS is not fully understood, but evidence of a genetic component has been recognized in family and twin studies.³ Oligo-ovulation or anovulation in women with PCOS is a major cause of infertility and such women might require ovulation induction

or assisted reproductive technology to become pregnant.⁵

Women with an isolated finding of PCO on ultrasonography without any other clinical or biochemical disturbances of PCOS probably form a different group of patients than women with signs of anovulation, hyperandrogenism and hyperinsulinaemia⁶. Changes to lifestyle can, however, improve the metabolic and endocrine consequences of having PCOS, thus possibly improving infertility caused by anovulation.⁷

The diagnostic criteria for PCOS have long been an issue of debate. However, a

much-needed consensus was recently reached at a congress of the European Society of Human Reproduction and Embryology (ESHRE) and American Society for Reproductive Medicine (ASRM) in Rotterdam on May 1–3, 2003, on the diagnostic criteria and long-term health risks related to PCOS. The newly revised criteria for the diagnosis of PCOS are: (two out of three) (i) oligo- and/or anovulation, (ii) clinical and/or biochemical signs of hyperandrogenism and PCO. Other aetiologies such as congenital adrenal hyperplasia, androgen-secreting tumours and Cushing's syndrome have to be excluded⁸.

Hirsutism is defined as male-pattern growth of terminal body hair in women in androgen-stimulated locations such as face, chest and areola⁹. The rate, pattern and distribution of hair growth at these sites is influenced by various factors including an individual's genetic makeup⁹. Idiopathic hirsutism is characterized by normal androgen concentration and lack of identifiable underlying disorders¹⁰. More than 95% women with hirsutism have PCOS and 20% have idiopathic hirsutism⁹.

Hyperandrogenism includes hirsutism and is considered as one of the major inclusion criteria for PCOS confirmation by Rotterdam consensus. This study was aimed to find the frequency and relation of PCOS with hirsutism.

PATIENT AND METHODS

It was a Cross-sectional Analytical Study. Females aged 14-20 years, registered at Outpatient Department of Dermatology, Sheikh Zayed Medical Complex, Lahore with and without symptoms of PCOS in accordance with FG score were enrolled in the study.

Females with virilism and cushing syndrome were excluded from the study. The sample size was estimated by using 95% confidence level, 90% power of study with reference value of PCO 70-80% among hirsute.⁴ The estimated sample size was 50 for each group.

Purposive non probability sampling technique was opted. After the clearance of Institutional Review Board of Sheikh Zayed Medical Complex, Lahore (IRB Ref No: 1003) fifty females with symptoms of hirsutism and 50 age matched females without hirsutism were enrolled in the study. The objectives of the study were explained to the females fulfilling the requirements of inclusion criteria. A written informed consent was

obtained. A semi-structured questionnaire which included questions related to their age, age of menarche, days of menstrual cycle, oligomenorhea and clinical history was filled. To see the degree of severity of hirsutism, they were divided into two groups A and B for 14-17 years and 18-20 years respectively. For age of menarche they were divided into a, b and c groups of ages 11-12, 13-14 and 15-16 years respectively. For each enrolled female, ultrasonography was done by a single radiologist for the functioning of ovaries and adrenals. Weight and height was recorded for BMI calculations. Hirsutism was scored in accordance with the modified FG score (no hirsutism: <8, mild hirsutism: 8-16, moderate hirsutism: 17-25, severe hirsutism: >25) to determine the severity of hirsutism by assessing the extent of hair growth at 9 key anatomical sites². PCO was diagnosed on the basis of ultrasound when at least one ovary had a volume above 10ml or there were 12 or more follicles measuring 2–9mm in diameter. Age below 13-14 years was considered as early menarche which was based on the reported data of menarche in Pakistan.¹¹

Each enrolled female was requested to come fasting between 8.00 am to 8.30 am on their next visit and 5 cc venous blood was drawn. Serum was separated and stored at –20°C till biochemical analysis of LH, FSH, free testosterone, cortisol, DHT and ALT.

LH and FSH were measured using Immunometric Assay kits from NETRIA (UK). The calibration range of both assays was upto 200mIU/ml with an analytical sensitivity of 0.02mIU/ml. Cortisol, free testosterone were analyzed using Enzyme Linked Immunosorbant Assay (ELISA) from Novatec (Germany). The calibration range of these analytes was 1380nmol/L and 100p/ml respectively. The analytical sensitivity of these assays was 5ng/ml and 0.06pg/ml respectively. DHT was analyzed using ELISA from IBL (Germany). The calibration range of assay was upto 2500 pg/ml. The analytical sensitivity of the assay was 6pg/ml. ALT was measured spectrometrically using assay kit from Fortress (UK). The detection limit was as low as 3U/L.

Sample handling and temperature conditions were strictly observed for all procedures according to manufacturer's instructions. For precision of assay, calibrated micro/multichannel pipettes from Gilson were used throughout the assay procedures and washing was performed with automatic plate

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washer. Analysis for reporting the hormonal levels was carried out using softmax statistical package. For diagnostic assurance of results, all investigations were carried out with 5-6 standards points and 2 quality control pools in each assay batch.

Data Analysis

Study data was analyzed using Statistical Package for Social Sciences (SPSS version 15.0 for Windows; SPSS Inc., Chicago, IL, USA). Analysis was carried out at three levels, descriptive, univariate and bivariate analysis. Descriptive statistics of socio-demographic variables were computed, mean ± SD was calculated for quantitative variables (age, age of menarche, and different hormonal functions test) and frequency for categorical variables (hirsutism, PCO, oligomenorhea and BMI categories). Independent sample t-test was used to compare hormone levels between PCO and non-PCO for hirsute and normal groups. Relation of severity of hirsutism with age and with duration of hirsutism was determined by

using Chi-square test. Value of $p \leq 0.05$ was considered significant.

RESULTS

A total of 50 females with hirsutism and 50 age matched without hirsutism aged between 14-20 years were enrolled in the study. Mean age of the study population was 18.4 ± 1.5 years.

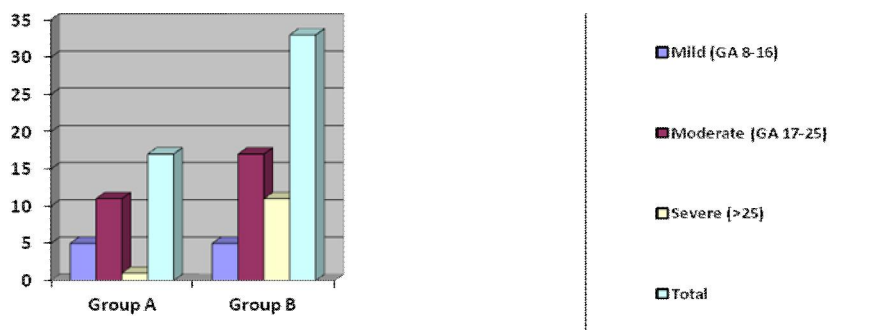
Seventeen (34%) females among hirsutes and 23(46%) among 50 normal females belonged to age group A. No significant difference was seen between the ages of two study groups ($p=0.221$). Twelve (24%) hirsutes and 6 (12%) of normal females had menarche at 11-12 years.

By using FG scores, study group was assessed for severity of hirsutism. Seventeen (34%) were in the age group A. Five females each from both age groups had mild hirsutism. Moderate to severe hirsutism was seen in 80% of hirsute females ($p=0.062$) (Fig 1).

Table 1: Mean age of menarche of study population was 13.4 ± 1.0 .

Study population	Age group (years)		Mean±SD (years)	Age of menarche (years)		Mean ±SD (years)	
	A(14-17)	B(18-20)		a (11-12)	b(13-14)	c(15-16)	
Hirsutes (n=50)	17(34%)	33 (66%)	18.3 ± 1.4	12 (24%)	29(58%)	9 (18%)	13.3 ± 1.1
Controls(n=50)	23(46%)	27(54%)	18.5 ± 1.5	6 (12%)	36(72%)	8 (16%)	13.5 ± 0.9

Figure 1: Severity of hirsutism according to FG score (n=50)



GA= Grading Assessment

Duration of onset of hirsutism ranged from 1-8 years. Forty-three (86%) had hirsutism for 1-5 years and 7 (14%) had history for 6-8 years.

Eleven (22%) hirsute and 6(12%) normal females were overweight (BMI >25) and 31 (62%)

hirsute and 34(68%) normals were within the normal weight limit (BMI 18.5-24.9). Among the hirsute cases 28 (56%) and 48 (96%) of controls had regular menstrual cycle. On ultrasonography 34(68%) hirsute females and 16(32%) normals had

PCO. None of the participant had adrenal anomaly. (Table 2)

Based on the hormonal levels it was seen that among the hirsute females with PCOS the LH:FSH ratio was more disturbed either in leuteal phase (2.8:1) or follicular phase (2.5:1) whereas among hirsute females with no sign of PCOS the LH:FSH

ratio was 1:1, regardless of menstrual phase, luteal or follicular. Among controls LH:FSH ratio was normal either in luteal or follicular phase. The levels of free testosterone, DHT, cortisol and ALT were normal in both groups. (Table 3)

Table 2: Frequency of menstrual cycle regularity, obesity &PCO (n=100)

*BMI=Body mass index, **Oligo=oligomenorrhea

Study population	Menstrual cycle		Obesity (BMI*)			PCO	
	Regular	Oligo** %	<18.5 (%)	18.6-24.9 (%)	>25 (%)	+ve (%)	-ve (%)
Hirsutes mild (n=10) Moderate (n=28) Severe (n=12)	4 (40%)	6 (60%)	1(10%)	6 (60%)	3 (30%)	5 (50%)	5 (50%)
	15(53.6%)	13(46.4%)	5 (17.6%)	18 (64.3%)	5(17.6%)	19(67.9%)	9(32.1%)
	9(75%)	3(25%)	2(16.7%)	7(58.3%)	3(25%)	10(83.3%)	2(16.7%)
Controls (n=50)	48(96%)	2(4%)	10(20%)	34(68%)	6(12%)	16(32%)	34(68%)

Table 3: Hormonal levels in hirsute and normal females (n=100)

PCO status	Hirsutes						Controls					
	N	LH:FSH		FT pg/ml	DHT Pg/ml	Cortisol nmol/l	N	LH:FSH		FT pg/ml	DHT Pg/ml	Cortisol nmol/l
		L*	F**					L	F			
+ve	3 4	2.8: 1	2.5: 1	2.0±1.3	345±17 4	283±19 0	1 6	0.9: 1	0.7: 1	1.9±1.4	326±71	320±11 7
-ve	1 6	---	1:1	1.63±0.8	297±21 1	226±11 7	3 4	0.6: 1	0.4: 1	1.5±0.6	330±16 2	291±11 0
Pvalue	--	--	--	P=0.27 1	P=0.39 6	P=0.27 4	--	--	--	P=0.30 2	P=0.91 4	P=0.41 4

(L* = Luteal Phase and F** = follicular phase)

Normal ranges: LH - F 2-18 mIU/ml, L 3-10 mIU/ml, FSH – F 2-10 mIU/ml, L 2-10 mIU/ml, LH:FSH 1:1, Cortisol- 138-635 nmol/L (morning), FT=Free Testosterone - 0.6-3.1pg/ml, DHT 24-368pg/ml

DISCUSSION

Hirsutism is a common endocrine disorder distressing young women. Its severity varies from mild to severe. The severity is assessed by semi-objective scoring system (Ferriman & Gallway Score). This scoring system allows a systematic follow up of the results of treatment. The abnormal metabolism of increased androgens in the hair follicles may result in excessive stimulation of hair

growth. Rarely a clearly defined pathological entity such as congenital adrenal hyperplasia or an androgen secreting adrenal or ovarian tumour is the cause of the androgen excess.¹² In majority of cases there is mild androgen excess causing hirsutism with or without disruption of regular ovulation.⁵ In current study hirsutism was seen in 66% females aged 18-20 years and 34% aged 14-17 years. Another study elsewhere reported 43.7%

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cases of hirsutism between 16-20 years and it seem that 18-20 years is the common age for expression of hirsutism¹³. A Kuwaiti study has documented the duration of hirsutism between 6 months to 14 years¹⁴. The results of current study presents history of hirsutism for 1-8 years, among them 40 (80%) of females had history of hirsutism for 2-5 years. Present study showed that the duration of hirsutism is related to age of menarche and severity is related to PCO positivity. Similar results were reported in another study where most forms of non-neoplastic hirsutism became evident around puberty and related to PCOS, congenital adrenal hyperplasia and idiopathic hirsutism in some cases¹⁵.

Using FG score, in the present study 10 (20%) cases had mild, 28 (56%) had moderate and 12 (24%) had severe hirsutism. Another study using the same classification reported 43.7% cases with mild, 37.5% with moderate and 15.6% with severe hirsutism¹⁴. This difference in staging of hirsutism could be due to geographical and ethnic variations.

In present study PCO was seen in 68% hirsute females and in 32% healthy control females. Thirty percent of females with PCOS had oligomenorrhea. Another study¹⁶ reported 18% prevalence of PCO in asymptomatic females, 37% among females either with oligomenorrhea or hirsutism and 70% who had both oligomenorrhea and hirsutism. Chhabra S reported PCO in 70% females with hirsutism.¹⁷

Previous studies have showed that women with oligomenorrhea and hirsutism have severe changes in hormonal profile and the reason for oligomenorrhea could be due to follicular disturbances^{13, 16}. In this study the follicular disturbances (LH: FSH ratio) was seen in 34(68%) of hirsute females.

Studies¹⁸ elsewhere have reported a strong relation among PCOS and obesity, hirsutism and PCO. However in the current study it was observed that out of the 50 hirsute females 11 (22%) were obese.

Increase in adrenocorticotrophic hormone in females due to stress and fatigue triggers the adrenal cortex which results in increase in cortisol levels. However, with chronic or repeated stress, the body continues to produce cortisol which weakens the adrenal gland and results in production of androgen in excess causing hirsutism.¹⁹ An increase in cortisol levels disturbs the balance of sex hormones in body, resulting into hirsutism or PCOS.¹⁹ We did not observe increase

in cortisol level in this study, though cortisol levels among hirsute females were found higher than control healthy females.

In present study, features of metabolic syndrome (liver dysfunction) were not disturbed in study participants. These features usually appear later in females life¹⁶. A study has shown that 15% women with PCOS have liver disease²⁰. The cause of hirsutism with normal levels of free testosterone could be idiopathic. Different studies have shown that androgens (testosterone and DHT) are elevated in 70-80% patients with hirsutism, conversely not all hirsute patients have detectable androgen excess as 5-15% of these women have idiopathic hirsutism²¹. In this study levels of ALT, free testosterone and DHT were normal in all cases.

CONCLUSION

The hirsutism is higher in females having PCO combined with oligomenorrhea than in cases with PCO alone.

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