Heterogeneity of the Polycystic Ovary Syndrome Clinical, Endocrinal and Ultrasound Features

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ABSTRACT

Aim: To find out the various clinical endocrinal and ultrasound features in patients who present with oligoamenorrhea and also to search for wide range of phenotypes of polycystic ovarian disease.
Methods: This prospective cohort study included 143 patients during duration from 1st January till 30th September 2013 presenting with features of oligomenorrhea and amenorrhoea. The percentage of various clinical and biochemical features of polycystic ovarian syndrome were studied at Gynae OPD of Shalamar Hospital.
Results: Hirsutism was present in 92 patients. 43.7% had mild while 24.3% had severe hirsutism, primary infertility was feature of these patients in 50.7% and secondary infertility 16.9%. 72.7% had increase in ovarian volume more than 10cm^3. Elevated LH manifested in 36.7% while hyper prolactineamia was detected in 29.5% while hypothyroidism was in 0.9%. Testosterone was elevated in 16.2% of 37 patients and androsteindion in 72.2% of 22 patients tested.
Conclusion: Polycystic ovary syndrome (PCOS) is a true syndrome, being a heterogenous collection of signs and symptoms that gather together to form a spectrum of disorder.
Keywords: Polycystic ovary syndrome, ultrasound, oligoamenorrhea

INTRODUCTION

Polycystic ovary syndrome is a true syndrome being a heterogeneous collection of signs and symptoms that gather together to form a spectrum of a disorder with a mild presentation in some, whilst in others there is a severe disturbance of reproductive, endocrine and metabolic functions[1]. The polycystic appearance of the ovary is the distinguishing sign of polycystic ovary syndrome but there is wide range of clinical and biochemical features, which includes, menstrual cycle disturbance, obesity, hirsutism, acne, and abnormalities of biochemical profiles including elevated serum concentrations of luteinizing hormone (LH), testosterone, androsteindion and insulin. Presentation of the syndrome is so varied that one, all, or any combination of the above features may be present[2].

There is considerable heterogeneity of symptoms and signs among women with PCOS and for an individual these may change over time[3]. PCOS is familial and various aspects of the syndrome may be differentially inherited[4]. There are no. of interlinking factors that affects the expression of PCOS. A gain in weight is associated with worsening of symptoms while wt loss ameliorates the endocrine and metabolic profile and symtomatololgy[5].

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The pathogenesis of polycystic ovaries and the associated syndrome is still being elucidated, but the heterogeneity of presentation of PCOS suggests that a single cause is unlikely. Recent genetic studies have identified a link between PCOS and disordered insulin metabolism and indicates that syndrome may be the presentation of a complex genetic trait disorder[6].

PATIENTS & METHODS

Patients with age range of 14-50 who presented in OPD of Shalamar Hospital with oligomenorrhea or amenorrhea for spectrum of this disorder. The clinical data included age, BMI, and the presence of acne and hirsutism, which was defined using ferriman and gallway, score. The menstrual cycle was described as being regular, oligomenorrhea (a cycle interval longer their 35days but less than 6 months) or amenorrhea (no menstruation for more than 6months). Marital status was identified and infertility as primary or secondary infertility of at least 1 year duration.

Transabdominal ultrasound in unmarried women and transvaginal in married was carried out, usually on day 10 to determine the ovarian volume and morphology. The criterion of 12 or more cysts of 2-9mm in diameter arranged around an echodense central stoma, and volume of >10ml, as described by Adams and colleagues was used to diagnose presence of polycystic ovaries[7].

Measurement of plasma levels of FSH, LH and testosterone and androsteindion were carried out. Every patient had TSH and prolactine level estimation to rule out other causes of amenorrhea/oligomenorrhea. 17α hydroxy progesterone and cortisol level were only performed where history suggestive of Cushing syndrome or late onset CAH, was present because of cost constraints.

Technique used for hormonal evaluation was chemiluminesence. For FSH 1.98-11.6miu/ml LH, 2.58-11.1miu/ml, Serum testosterone 5.7-77ng/dl for androsteindion 0.3-3.5mg/ml. SHBG 18-114n mol/l, Serum prolactin 3.0-18.6ng/ml, TSH 0.4-4.68, for 17-OH progesterone 0.2-13ng/ml were be taken as normal ranges. These tests were performed or 2nd or 3rd day of menstrual cycle or any index day of amenorrhoeic phase.

A serum follicle stimulating hormore (FSH) concentration of greater than 15min/ml that is not associated with pre ovulatory surge of (LH) suggests impending ovarian failure, while FSH levels of greater than 40min/ml are suggestive of irreversible ovarian failure.

A patient with serum prolactin concentration greater then 100ng/ml underwent computed tomography (CT) or magnetic resonance imaging (MRI of the pilutary fossa to exclude a hypothalamic tumor or nonfunctioning pituitary tumor.

Since this was descriptive study, no inferential tests of P value was required. Descriptive statistics were applied by SPSS version 11.0 mean values and 5th –95th percale were determined the percentages and frequency of clinical and laboratory variable were determined.

RESULT

Five patients were excluded because of premature ovarian failure. Two patients with hyperprolactineamia more than 100ng/ml were excluded and further investigated. Total 136 patients were included in the present study.

Table I depicts the characteristics of women presenting with oligoamenorrhea. Mean age was 24.7 and range of BMI was 15-54. Mean ovarian volume was 10.1 and range was 2.5-20. While 5th – 95th percentile ranged between 3.2-17.9ml^3.

Table II manifests the spectrum of clinical manifestation and biochemical features and their frequencies and valued percentage. Menstrual irregularity was present in 136 patients 33.7% had oligomenorrhea while 34.6% had amenorrhea and 16% presented with hypomenorrhea.

Hirsutism was present in 92 patients which was mild in 43.7% and of moderate degree of severity in

24.3%. 76.5% of patients presented with increase in weight, Acne were present in 25.9% of patients. Primary infertility manifested in 50.7% of patients while secondary infertility was present in 16.9%. 72.7% of patients were diagnosed with increase volume of ovaries more than 10cm^3.

Elevated LH was present in 36.7% while hyper-prolactineamia was present in 29.5% Hyperandrogeneamia testosterone was elevated in 16.2% of 37 patients and andresteindion was elevated in 72.7% of 22 patients tested. While hypothyroidism was detected in 0.9% of patient graph III in figure shows the relationship of BMI with infertility, LH level and hirsutism. As the women achieved higher BMI the frequency of infertility increased. In grossly obese women with BMI >39-42 the level of infertility reached to 83% hirsutism also became more severe with increase in weight. LH was elevated in overweight and obese women - This elevation was more marked in BMI range of >36-39.

Table I: Characteristics of 136 women presenting with oligoamenorrhea and ultrasounded detected PCO Ovaries.

	Mean	Normal range	5-95 Gentile
Age (yrs)	24.7	13->39	17-33
Body mass index kg/m^2	28.47	<15-54	20.3-402
Ovarian volume cm^3	10.1	2.5-20	3.2-17.9
Follicle stimulating H	5.1	2.1-10.4	2.6-7.8
Luteinizing hormone	10.1	12.2-33	2.9-206
Prolactine	15.8	0.1-60	6-34.2
Thyroid Stimulating H	1.8	02.5-9	0.65-3.1
Testosterone	43.2	0.6-97.7	0.6-906
Androsteindion	8.7	0.2-20.2	0.22-20.02

Table II: The Spectrum of Clinical Manifestation of the Heterogeneous Polycystic Ovarian Syndrome   (n=136.)

Symptoms	Frequency	Valid %age
Oligomenorrhea	73	53.7
Amenorrhea	47	34.6
Hypomenorrhea	16	14
Hirsutism		
Mild	59	43.7
Moderate	33	24.3
Increase in weight	104	76.5
Galactorrhea	6	4.4
Acne	35	25.9
Infertility		
Primary	60	50.7
Secondary	23	16.9
Increase in ovarian volume	80	72.7
Increased LH	47	36.7
Testosterone	6	16.2
Androsteindion	16	72.7
Hypothyriodism	1	0.9%
Hyper Prolactineanmia	33	29.5%

Graph I: Relationship of BMI with percentage of infertility, Hirsutism and LH levels
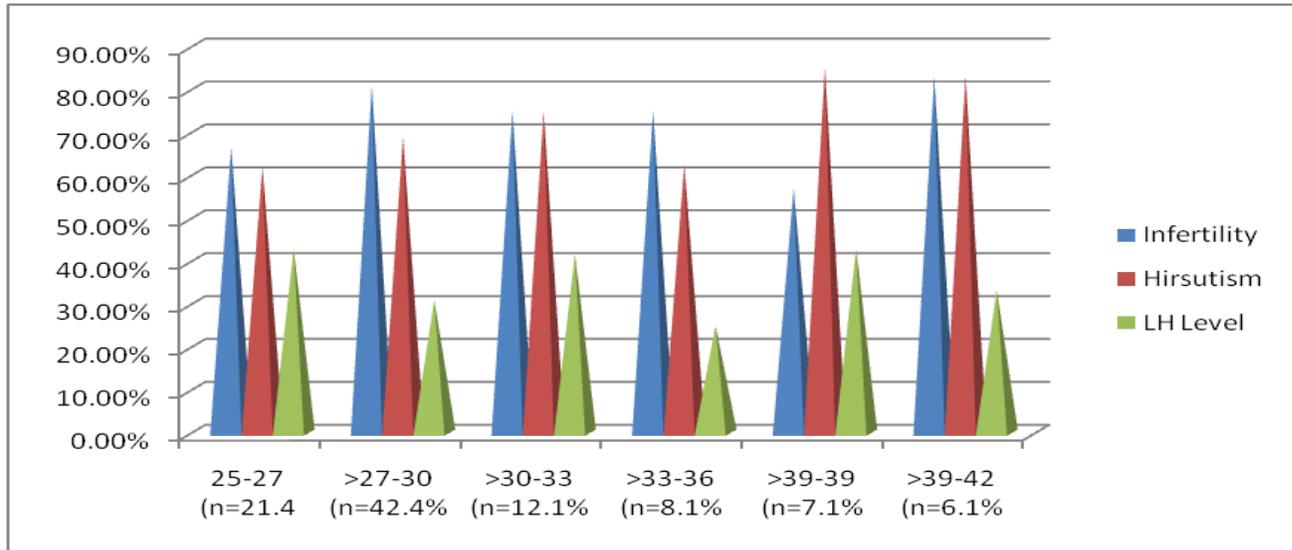
DISCUSSION

This study of 136 women shows that obesity is associated with increased risk of hirsutism and infertility. Obesity is also associated with elevated levels of LH.

Balen et al[3] in his study 1741 found significant association between increased BMI and hirsutism and menstrual cycle disturbance.

In this study classical endocrinal features of raised serum LH and testosterone were found in 36.7% and 16.2% respectively as compared to Balen et al[3] study although LH level was comparable in 39.8% but testosterone was elevated in 16.2% as the test of testosterone were carried out only in 37 patients. Many other groups have similarly reported heterogeneity in their population with PCO for example Frank[8] reported elevated LH in 51% and testosterone in 50% of patients.

Present study manifested elevated prolactine level in 29.5% of patients while Balen et al[3] is study observed 12% and Frank[7] in 7% of patients. The biochemical features of these women with PCO are not easily compared as criteria for elevated serum concentration of LH, testosterone and prolactine and their method of assessment are not consistent between studies.

In another series of women with oligomenorrhea independent correlations with ovarian morohology were identified with elevated LH concentrations and androgens level[9].

In this study 26% of patients with primary infertility and 14% of patients with secondary infertility had a BMI >30kg/m^2. 53.7% patient had oligomenorrhea while 34.6% had amenorrhea. In the present study increased ovarian volume was present in 72.7% of the patients. Conway[10] also demonstrated a higher mean ovarian volume in women with ultrasound diagnosed polycystic ovaries compared with control group in addition, Franks[8] with larger number of controls, demonstrated significantly larger uterine area, and nearly double mean ovarian volume in the PCOS group.

PCOS is, by its nature, a concurrent set of symptoms, signs, and biochemical features that can occur in various combinations. Consequently there is no single diagnostic marker, weather biochemical or genetic, to provide a gold standard for reference[11].

Two or Three criteria have to be met for the definition of PCOS: Chronic anovulation, clinical and/or biochemical evidence of hyperandrogenenism, and poly cystic ovaries. The main issues that continue to promote passionate discussion are first wether hyperandrogenemic women with polycystic ovaries and regular cycles should be included in the definition, and second, and perhaps more contentiously, wether women with polycystic ovaries and chronic anovulation without evidence of androgen excess should be defined as part of syndrome[12].

Women with polycystic ovaries, hyperandrogenism and regular cycles are less likely to have insulin resistance and hyper-insulineamia than those chronic anovulation[13].

The burgeoning evidence for including ovulatory women with polycystic ovaries and hyperandrogensim in the definition of PCOS was a major factor in motivating the European society for

human reproduction and Embryology/American society for reproductive medicine workshop.

Regarding the issue of women with polycystic ovaries and chronic anovulation but without clinical evidence of androgen excess, can be shown to have polycystic ovary syndrome. There are few systemic studies there have addressed this issue, but limited evidence to date favors inclusion of this subgroup within definition of PCOS[11].

The Rotterdam criteria[14] for definition and diagnosis of PCOS represents a significant advance in recognizing the broad spectrum of presentation of the syndrome, and acknowledges that the clinical and biochemical features may vary with time within individuals.

This study had small sample size to reach the statistical significant between various symptoms. A larger study is underway.

CONCLUSION

Obese women with PCOS are more likely to be anovulatory than lean, hyperandrogenemic subjects[15]. Weight gain is associated with an increasing chance of chronic anovutation.

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