



Clinical correlation with biochemical status in polycystic ovarian syndrome

Bhattacharya Dipankar, Mandal Salil Kumar, Mukherjee Satinath, Pradhan Mamata

Department of Physiology, University College of Medicine, Calcutta National Medical College Hospital

OBJECTIVE(S) : To correlate hormonal and anthropometrical data of patients with polycystic ovarian syndrome (PCOS).

METHOD(S) : Seventy women (12-35 years of age) with PCOS based on clinical suspicions were compared with 10 normal women.

RESULTS : Mean body mass index (BMI) was 21.6 kg/m² in normal women, 27.44 kg/m² in overweight subjects (n=44) and 31.86 kg/m² in obese subjects (n=21). Mean waist : hip ratio (WHR) was 0.82 in normal women and 0.83 in subjects. Seventy percent subjects were overweight, among whom 46.93% had high LH: FSH ratio, 59.18% had hyperandrogenism and 44.2% were hirsute, having significantly high BMI and total testosterone (TT). Sixty percent subjects were hyperandrogenic with high basal insulin BI in 35.7%. 62.8% fulfilled sonographic criteria for diagnosing PCOS - 70.45% of them bilateral, 22.72% only left-sided and 6.81% only right sided. 59.3% were hirsute and 38.6% hyperinsulinemic (BMI and TT were significantly high). A positive predictive value for TT was 64.44% and for LH: FSH 55.55%.

CONCLUSION(S) : High TT level is the single most diagnostic criterion. Hyperinsulinemia is related to hyperandrogenism. Bodyweight was related to ovarian stroma and hirsutism. Bengali women have lower bodyweight, but have more abdominal obesity. Ultrasonography is sensitive, but not specific for diagnosis of PCOS. Left ovary is affected more often in unilateral involvement.

Key words : polycystic ovarian syndrome, luteinising hormone, follicle stimulating hormone, total testosterone, ultrasonography, body mass index, basal insulin

Introduction

Polycystic ovarian syndrome (PCOS) is a syndrome of oligomenorrhea, hirsutism, and polycystic ovary with chronic anovulation and varying degrees of androgen excess. In anovulatory women, 75% have PCOS, though ultrasonography (USG) diagnosed cases may show normal hormone levels¹. Macroscopically, affected ovaries are smooth and sclerotic, have thickened capsule, capsular and subcapsular follicular cysts with varying atresia, and hyperplastic theca and stroma. Unaffected ovaries may also show similar changes.

Circulating estradiol is not like that in the follicular phase but estrone is elevated due to peripheral conversion and LH amplitude is increased more than its pulse and frequency². Due to estrogenic environment of anterior pituitary, a high

LH and low FSH occur. This is also due to decreased central opioid tone in hypothalamus in the absence of progesterone³. In PCOS, there is 50% reduction of serum hormone binding globulin (SHBG) due to increased testosterone and hence, free estradiol rises though the major fraction is peripheral estrone⁴. Free estradiol is correlated with LH:FSH ratio. Follicular FSH is suppressed by inhibin B and hence, new follicles form but not to a point of full maturation and ovulation⁵. Granulosa cells undergo atresia and patches of luteinized thecal cells are found in stroma. Granulosa cells are more sensitive to FSH. They are arrested in maturation.

In PCOS, high androgen causes insulin resistance and acanthosis nigricans is a marker for its severity. These women show android obesity with fat in the anterior abdominal wall and mesentery. This fat is metabolically more active and sensitive to catecholamines and less to insulin. Waist:hip ratio (WHR) varies inversely with serum high density cholesterol and hence these women are more prone to cardiovascular disease. Higher concentration of insulin binds to IGF-1 receptor of theca cells causing high androstenedione and testosterone. Again, high insulin decreases SHBG contributing to hyperandrogenism⁶.

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Correspondence :

Dr. Dipankar Bhattacharya

93/C, Regent Estate, Kolkata - 700 092.

Tel. 033-2412-5582, 2416 6632

Mobile (0) 9830025227 Email : dipbhatta@yahoo.com

PCOS presents with various clinical features like infertility, oligomenorrhea, hirsutism, alopecia and acne, but demonstration of anovulation is not necessary for diagnosis. This study was aimed at finding out a single diagnostic criterion for detecting PCOS at an early age.

Material and Methods

The study was done on outdoor patients over a period of 2 years from April 2001 to March 2003. Seventy women with PCOS diagnosed by history and hormonal levels (LH:FSH ratio ≥ 2 , total testosterone > 0.76 ng/mL) and ultrasonography (USG) (cortical cysts each 5 mm in diameter, > 5 in number in a single ovary) were compared with 10 normal women who served as control. Detailed history of menstruation and hyperandrogenic problems was recorded and clinical examination done. Obesity was measured by body mass index (BMI) (> 25 kg/m² taken as overweight). Waist: hip ratio (WHR) was used as a marker of abdominal obesity (measured at ASIS). Ferriman-Gallway (FG) scoring was done and a score of ≥ 8 was taken as significant hirsutism. USG was done with 3.5

MHz trans-abdominal probe. LH was measured by ELISA (Herrickson Diagnostics, Texas, USA), and FSH by ELISA (Genzyme Diagnostic Medix, Biotech, CA, USA). Total testosterone (TT) was measured by chemiluminiscence (CLIA) kit supplied by Ciba Corning Diagnostic Corporation. Statistical analysis was done with Student's t test using Microsoft Excel.

Results

Table 1 shows that the controls (n=10) had a mean age of 21.9 years, mean height 158.5 cm, mean weight 53.9 kg, mean BMI 21.63 kg/m², mean WHR 0.82, mean basal insulin (BI)/34.8 μ IU/mL, mean LH 5.04 mIU/mL, mean FSH 3.78 mIU/mL, mean LH:FSH ratio 1.34 and mean testosterone 0.54 ng/mL. (Table 1).

Table 2 shows hormonal status and BMI in PCOS individuals who were overweight (49 out of 70 cases). They had a mean BMI 28.98 kg/m², mean basal insulin (BI) 33.49 μ IU/mL, mean LH:FSH ratio 2.01, mean testosterone level 1.38 ng/mL (Figure 1).

Table 1. Hormonal status, BMI, Waist:Hip ratio in normal female individuals (n=10)

	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m ²)	Waist:Hip ratio	BI (μ IU/mL)	LH (mIU/mL)	FSH (mIU/mL)	LH:FSH ratio	Testosterone (ng/mL)
Mean	21.9 \pm 3.07	158.5 \pm 6.52	53.9 \pm 2.13	21.63 \pm 1.18	0.82 \pm 0.06	34.8 \pm 9.37	5.04 \pm 0.8	3.78 \pm 0.37	1.34 \pm 0.15	0.54 \pm 0.1
Range	17 to 26	148 to 167	51 to 58	10.8 to 23.5	0.81 to 0.83	25 to 48	4.2 to 6.3	3 to 4.3	1.16 to 1.60	0.5 to 0.8

BMI - Body mass index LH - Lutinising hormone BI - Basal insulin FSH - Folicle stimulating hormone

Table 2. Hormonal status and BMI in overweight (BMI > 25 kg/m²) PCOS individuals (n=49)

	BMI (kg/m ²)	Basal inulin (μ IU/mL)	LH:FSH ratio	Testosterone (ng/mL)
Mean	28.98 \pm 3.11	33.49 \pm 13.32	2.01 \pm 1/46	1.38 \pm 1.34
Range	2.5 to 39	6.45 to 56.21	0.31 to 4.6	0.05 to 4.5

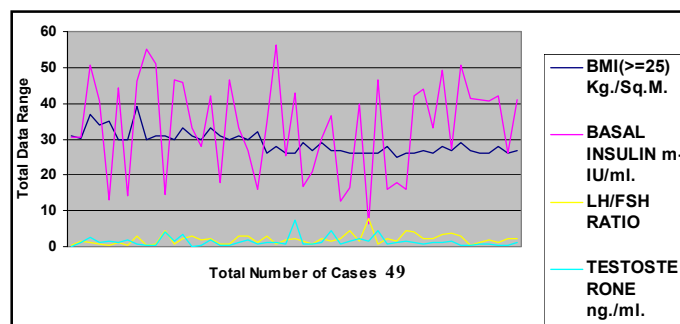


Figure 1. BMI-BI-LH:FSH-Testosterone in overweight PCOS individuals.

Out of the 70 cases with PCOS 31 (44.2%) had hirsutism . Within these, 35.4% were overweight (BMI > 25 kg/m²) and 40% obese (BMI > 30 kg / m²). Increased value of basal insulin, LH:FSH ratio, testosterone and positive family history (presence of PCOS in mother or sister or both) were found in 14 (45.16%), 16 (51.6%), 20 (64.5%) and 7 subjects (22.5%) respectively. In this group, mean BMI was 29.24 kg/m², mean BI 32.94 m IU/mL, mean LH:FSH ratio 1.96 and mean testosterone 1.76 ng/mL. (Table 3; Figure 2).

Table 4 shows comparison of hormone levels in two groups in study population - one group with significant hirsutism and

Table 5. Hormonal status and BMI in sonographically determined PCOS individuals (N=45)

	Body Mass Index (kg/m ²)	Testosterone (ng/mL)	LH:FSH ratio	Basal insulin (µIU/mL)
Mean	28.9±3.37	1.34 ± 1.31	2.09 ± 1.44	31.84 ± 14.16
Range	20 to 35	0.005 to 4.02	0.31 to 4.6	6.4 to 58.5

Both ovaries were involved in 34, only right ovary in 3 and only left ovary in 8

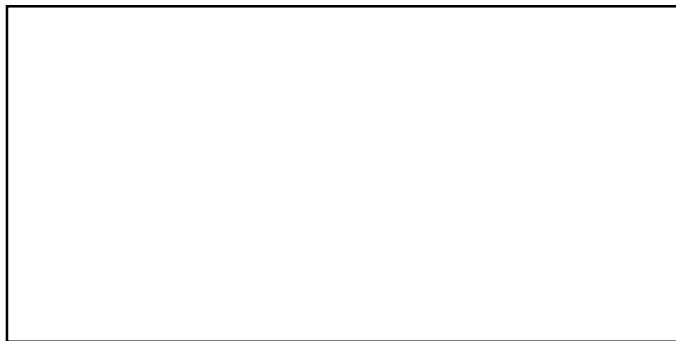


Figure 3. Testosterone-LH:FSH in sonographically diagnosed PCOS individuals.



Figure 4. Testosterone - LH:FSH in 42 PCOS individuals.

Table 6. Relation of high testosterone (>0.76 ng/mL) and other hormones in PCOS

	Testosterone (ng/mL)	LH:FSH ratio	Basal insulin (mIU/mL)
Mean	1.91 ± 0.21	2.50 ± 4.14	30.18 ± 13.43
Range	0.82 to 4.02	0.42 to 4.60	6.46 to 56.21

On ultrasonography both ovaries were involved in 20, only right in 2, only left in 7 and none in 13

Discussion

In the present study, the normal population showed the mean height of 158.5 cm, mean weight of 53.9 kg and mean BMI of 21.6kg/m². Earlier studies done upon the population of western countries⁷ showed a mean BMI of 25.9kg/m². In our study the mean waist:hip ratio was found to be 0.82, in comparison to the western group having the mean ratio of 0.77⁷; the mean LH level was 5.04 mIU/mL in comparison to the western data showing 4.1 mIU/mL. Similarly, the mean FSH level was 3.78 mIU/mL, while in western findings it was 4.9 mIU/mL⁷. The mean LH:FSH ratio was 1.34 in the present study, whereas it was 0.9 in the western group⁷. The mean total testosterone level was 0.64 ng/mL, whereas the western group showed the same as 1.2 ng/mL⁸ (Table 1). The above data suggested that the Indian population (Bengali women) has a lower body weight but with increased abdominal fat in comparison to western group and both LH:FSH and hyperandrogenism are less in our population.

Forty-nine out of the 70 subjects were overweight with mean BMI of 28.98±3.11 kg/m² as against 21.63±1.18 kg/m² in the

controls (P value=0.001) implying significant increase in comparison to the control group. LH:FSH ratio was 2.01± 1.46 in the overweight group as against 1.34 1.54 ± 0.15 in the controls (Table 1 and 2).

42.22% (19/45) USG diagnosed PCOS subjects had significant hirsutism (FG ≥8). In this hirsute PCOS subset, high BMI was found in 35.4%, high BI in 40%, high LH:FSH ratio in 51.6% and high testosterone in 64.5%. By Student’s t-Test, it was derived that BMI was very significantly high (P<0.0002; 29.24 ± 4.78 vs 21.67 ± 1.18) and testosterone value significantly high (P < 0.01 ; 1.76±1.51 vs 0.54 ± 0.1) than that in the control. It supports the idea that LH produced increased androgen by thecal stimulation, which in turn, caused hirsutism⁹. It also supports the result of an earlier study done in the Kashmir valley of India that PCOS was a cause of hirsutism in 37.3% of the Indian population¹⁰. Western study also showed high testosterone level in hirsute subgroup (>95th percentile of normal). Greater body mass in hirsute group was also the result of high testosterone causing obesity⁹.

According to NIH-NICHHD criteria for diagnosis of PCOS (set in 1990), USG was not mandatory¹¹. Western data showed that around 50% of biochemically diagnosed PCOS had fulfilled USG criteria¹². It was done for comparison of hormonal levels in the present study. 62.8% or 45 of 70 subjects demonstrated the USG proof of diagnosis and of them, 70.45% had bilateral involvement. Only left side was involved in 22.72% and only right side in 6.81% of the USG detected PCOS subjects. This implied that if only a single ovary is involved, there is a propensity for left-sided involvement.

In the present study, within the USG detected group F-G score \geq 8 was found in 68.88% (31/45). In this group of 31, high BMI was found in 68.88%, high testosterone in 64.44%, high LH:FSH ratio in 55.55% and high BI in 37.77%. The mean values of this subset were BMI 28.9kg/m², BI 31.64mIU/mL, LH:FSH ratio 2.09 and testosterone 1.34 ng/mL. The above data implied that USG proved subjects of PCOS also showed biochemical diagnostic parameters like LH:FSH ratio, hyperandrogenemia and excess body weight. On statistical analysis, BMI increase was highly significant (P<0.0002).

In the western study of USG detected PCOS cases, it was found that obesity was present in 50% PCOS subjects. In USG detected cases significant correlation was found with hyperandrogenism¹³. Earlier data also showed significant increment in LH:FSH ratio in USG detected PCOS subjects⁷. BI was found to have a direct correlation with ovarian stroma, which was increased in polycystic ovaries. A higher value of testosterone without any USG evidence of PCOS was found in six cases of PCOS in the present study. Therefore, USG is a sensitive but not specific diagnostic modality.

In subjects fulfilling the diagnostic criteria of PCOS on USG, it was found that positive predictive value of high total testosterone was 64.44% and of LH:FSH ratio 55.55%. These observations suggest that testosterone could be taken as a single most reliable parameter for the diagnosis of PCOS in preference to LH:FSH ratio. Earlier, it was shown that LH:FSH ratio and fasting insulin level, in a combined way, were of higher predictive value in diagnosing PCOS¹⁴.

When testosterone was taken as a diagnostic marker, 60% of subjects showed high value, a direct contradiction to the 30% value in an earlier study done in India¹⁵. In our hyperandrogenemic group, mean testosterone was 1.91 ng/mL and mean LH:FSH ratio 2.5. These higher than normal values of testosterone and LH:FSH ratio suggested greater correlation of both the parameters in polycystic ovarian syndrome. Therefore, it is suggested that it will be an accurate and cost-effective approach towards diagnosis for PCOS, if estimation of testosterone with LH:FSH ratio is taken as an independent

parameter. Again BI was high in the hyperandrogenemic group in 35.7% of cases. This supports the concept that higher insulin level inhibits ovulation and produces more ovarian androgen from the thecal cells, which in turn, causes hirsutism. In overweight PCOS patients, high testosterone reflects the concept of androgen causing more obesity⁹.

Thus high total testosterone level is the single-most diagnostic criterion for PCOS. Hyperinsulinemia is related to hyperandrogenism. Bodyweight is related to ovarian stroma and hirsutism. Bengali women are of lower bodyweight, but have more abdominal obesity. USG is sensitive but not specific for diagnosis of PCOS. Left ovary is affected more often than right in unilateral involvement.

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