Sonographic parameters and hormonal status in lean and obese women with polycystic ovary syndrome

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Summary

A total of 34 patients with the diagnosis of polycystic ovary syndrome (PCOS) were recruited for this study. Weight distribution in lean PCOS women (n=17) was 93.5% to 110.5% of normal weight for height and age. In obese women (n=17) this distribution was 119.5 to 146.5%. Serum testosterone (T), dehydroepiandrosterone sulfate (DHEA-S), Δ4-androstendione (Δ4-A), sex hormone binding globulin, (SHBG), 17-hydroxyprogesterone (17-OH PRG), 17b oestradiol (17b-E2), cortisol (CORT), follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL) and insulin (INS) were measured. Serum SHBG levels were lower in obese PCOS women (72.9±16.2 nmol/l) than in lean PCOS women (99.6±10.5) ($p<0.001$). Fasting insulin levels were higher in obese PCOS women (30.4±4.5 mUI/ml) than in lean PCOS women (14.2±7.6 mUI/ml) ($p<0.001$). Mean ovarian volume did not differ significantly between lean and obese PCOS women (12.5±3.7 ml vs 16.1±5.3, $p>0.5$). Endometrial thickness was roughly similar between the two groups. Endometrial surface area in lean PCOS women (7.6±2.2 cm^2) was lower than in obese PCOS women (10.1±1.9 cm^2) and the difference was significant ($p<0.01$).

Key words: PCO; Hormonal status; Sonography findings.

Introduction

Polycystic ovary syndrome (PCOS) is the most common disorder in women of reproductive age [1], characterized by hyperadrogenism and chronic anovulation [1, 2]. Its etiology remains unknown. However, PCOS may be manifested by a variety of clinical presentations. Symptoms may range from acne and mild hirsutism to oligomenorrhea, amenorrhea, infertility and severe generalized hirsutism.

Ultrasound scan allows morphological assessment of the ovaries and sonographic appearance of polycystic ovaries has become an important criterion for PCOS diagnosis [3]. The typical polycystic pattern was defined by the presence of ≥ 10 cysts measuring 2-8 mm in diameter arranged peripherally around a dense core of stroma or scattered through an increased amount of stroma [3, 5]. Ovarian enlargement is considered a marker of excessive androgen production and disturbances of the menstrual cycle in PCOS [4].

PCOS may be an incidental finding on a routine ultrasound scan in a women of normal weight with regular cycles, who do not exhibit signs of hyperandrogenism or conversely, these women may present a classical appearance of hirsutism, obesity and oligo- or amenorrhea. The most important abnormality in patients with PCOS is one of anovulation manifested by oligomenorrhea or secondary amenorrhea. The sonographic appearance of PCOS may occur together, or in isolation with a biochemical status, which involves metabolic and hormonal changes [6]. Concentrations of luteinizing hormone (LH) are elevated in 45-75% of cases and raised testosterone levels are seen in 80% of patients. The above hormonal levels are the usual indicators of the syndrome.

Obesity is very common among women with PCOS and 30-60% are overweight to some degree [7]. The comparisons of hormonal status between obese and normal weight women with PCOS have yielded conflicting results but it seems that obesity does not increase the prevalence of hirsutism and anovulation when compared to non-obese women with PCOS [8].

The purpose of the present study was to evaluate obese PCOS women compared to lean PCOS women, with respect to various hormonal and sonographic parameters.

Materials and Methods

Subjects

A total of 34 patients with the diagnosis of PCOS were recruited for this study. Inclusion criteria were: (I) age 18-27 yrs, (II) no excessive exercise (>1 h/day), (III) no aggressive dieting (loss of >1 kg/week), (IV) no disease affecting gonadotropin or sex steroid hormone secretion, clearance or excretion, (V) no prior history of ablative ovarian surgery, chemotherapy or radiation and (VI) no hormonal therapy within 3 months of the study.

If serum 17a-hydroxyprogesterone was >5 ng/ml, an ACTH stimulation test was done to exclude patients with adrenal hyperplasia. If serum cortisol was >5 μg/100 ml and the dexamethasone suppressing test was abnormal, women were also excluded from the study.

Weight distribution in lean PCOS women (n=17) was 93.5% to 110.5% of normal weight for height and age. In obese women (n=17) this distribution was 119.5 to 146.5%. Patients were matched for age in the two groups.

The diagnosis of PCOS was made on the basis of hyperadrogenism and oligomenorrhea/amenorrhea/irregular cycles.

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Regular (normal) menstrual cycles were defined as cycles with a minimum-maximum length variation of < 4 days and with an intermenstrual interval between 21 and 35 days. Irregular cycles were those with length variation of ≥ 4 days and an intermenstrual interval of more than 35 days. Oligomenorrhea was defined as menstruation with an interval of > 35 days and amenorrhea as the absence of periods for ≥ 6 months. Infertility and hirsutism were present at varying degrees in some patients, but were not a requirement for the diagnosis.

Ovaries were ovulated by the use of transabdominal sonography with a 5-MHZ probe. Follicles appeared as round translucent structures. The mean follicle number was calculated as the addition of left and right divided by two. The ovarian volume was estimated according to the following formula: 1/2 (AxBxC), where A is the longitudinal diameter of the ovary, B the anteroposterior diameter and C the transverse diameter of the ovary. Mean ovarian volume was calculated as the addition of left and right divided by two. Ovarian stroma volume was estimated according to the same formula and total stroma count was calculated as the addition of left and right. Endometrial measurements were obtained in the longitudinal view of the uterus. The endometrium was measured from basalis to the contralateral basalis and endometrial thickness (mm) was obtained. Additionally, an endometrium surface area (cm^2) was obtained for all the women and the mean value for lean and obese PCOS women was calculated.

Hormone assays

We measured serum testosterone (T), dehydroepiandrosterone sulfate (DHEA-S), Δ4-androstendione (Δ4-A), sex hormone binding globulin (SHBG), 17-hydroxyprogesterone (17-OH PRG), 17b oestradiol (17b-E2), cortisol (CORT), follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL) and insulin (INS). All blood samples were drawn in the first 5 days of spontaneous bleeding or a progesterone induced withdrawal bleeding (Provera, 5 mg twice daily for 7 days).

Serum LH, FSH, PRL and INS concentrations were determined by specific immunoradiometric assays (IRMA). Serum androgen and oestradiol concentrations were determined by radioimmunoassays. SHBG was analyzed by fluoroimmunoassays.

Statistical analysis

The results were analyzed by the Student's t-test for unpaired data. Statistical significance was considered to be achieved at $p<0.05$.

Results

Table 1 summarizes patient data with respect to age and body weight. Patients were matched for age in the two groups, but there was a significant difference in terms of weight.

Table 2 summarizes the serum hormonal levels in both groups. The concentrations of LH, FSH and PRL did not differ significantly between the two groups. Serum T was not significantly different in either group (105.5±37.1 ng/dl in lean PCOS women and 91±40.3 ng/dl in obese PCOS women, p>0.05). Deydroepiandrosterone sulfate levels were also similar in the two groups (3908±1834 ng/ml in lean PCOS women and 3852±1750 ng/ml in obese PCOS women, p>0.05). Δ4-Androstendione levels in lean (1.6±0.9 ng/ml) and obese PCOS women (2.4±0.8) were similar, p>0.05. Serum E2, 17-OH PRG and cortisol were not significantly different in the two groups. Serum SHBG levels were lower in obese PCOS women (72.9±16.2 nmol/l) than in lean PCOS women (99.6±10.5) ($p<0.001$). Fasting insulin levels were higher in obese PCOS women (30.4±4.5 mUI/ml) than in lean PCOS women (14.2±7.6 mUI/ml) ($p<0.001$).

Table 3 summarizes the sonographic parameters (mean follicle number per whole ovary, mean ovarian volume, total stroma volume, endometrial thickness, endometrial surface area) of lean and obese PCOS patients.

Mean ovarian volume did not differ significantly between lean and obese PCOS women (12.5±3.7 ml vs 16.1±5.3, p>0.05). Total stromal volume in lean PCOS women (14.1±3.8 ml) and obese PCOS women (12±7.9 ml) was not significantly different. Endometrial thickness was roughly similar between the two groups. Endometrial surface area in lean PCOS women (7.6±2.2 cm^2) was lower than in obese PCOS women (10.1±1.9 cm^2) and the difference was significant ($p<0.01$). Lean and obese PCOS women did not differ significantly with respect to mean follicle per ovary (14±2.3 vs 17±5.2).

Table 1. — *Patient data with respect to age and body weight.*

	Lean PCOS women	Obese PCOS women	p
*Age (yrs)±SD	21.7±3.4	22.4±4.3	>0.5
**BW (%)±SD	102.0±8.5	133.1±13.5	<0.001

*Values are means ± SD.
** BW: Body Weight=percentage of the normal weight for height and age.

Table 2. — *Hormonal levels in lean and obese PCOS women.*

		Lean PCOS (n=17)	Obese PCOS (n=17)	p
LH	mIU/ml	13.7±9	13.3±7.2	>0.05
FSH	mIU/ml	5.2±2	5.7±7.2	>0.05
LH/FSH	Ratio	2.5±1.3	2.1±1.6	>0.05
PRL	ng/ml	8.4±3.1	9.7±4.2	>0.05
T	ng/ml	105.5±37.1	91.0±40.3	>0.05
Δ4A	ng/ml	1.6±0.9	2.4±0.8	>0.05
E2	pg/ml	128.6±34.8	114.5±44.8	>0.05
DHEA-S	ng/ml	3908.0±1834	3852.0±1750	>0.05
SHBG	nmol/l	99.6±10.5	72.9±16.2	<0.001
CORT	μg%	11.0±6.3	9.4±4.6	>0.05
17-OH PRG	ng/ml	2.2±0.9	1.9±0.8	>0.05
INS	mIU/ml	14.2±7.6	30.4±4.5	<0.001

Table 3. — *Sonographic parameters of lean and obese PCOS patients.*

			p
Endometrial thickness (mm)	8.2±3.5	8.1±2.3	>0.05
Endometrial surface area (cm^2)	7.6±2.2	10.1±1.9	<0.01
Total stromal volume (ml)	14.1±3.8	12.0±7.9	>0.05
Mean ovarian volume (ml)	12.5±3.7	16.1±5.3	>0.05
Mean follicle number	14.0±2.3	17.0±5.2	>0.05

Discussion

The comparisons of hormonal status between lean and obese PCOS women have yielded conflicting results [9-11]. In some studies, the concentration of LH appears lower in obese than in lean PCOS women. In the present study the difference was not significant.

As far as androgens are concerned, studies have not demonstrated any significant differences between lean and obese PCOS women [10]. In the present study androgen levels were similar between the two groups in agreement with previous studies.

One of the differences between lean and obese PCOS women was represented by SHBG. Obese PCOS women had lower sex-hormone binding globulin (SHBG) concentrations with respect to their non-obese counterparts. A few previous studies [12, 13] confirmed this correlation and found that weight loss was associated with a significant increase of SHBG.

Fasting insulin serum levels were higher in obese PCOS women in agreement with the results of previous studies [14], secondary to increased basal insulin secretion rates [15]. Additionally, insulin responses to an oral glucose load are increased in both lean and obese PCOS women [14].

Results of in vivo studies suggest that insulin regulates SHBG not only in obese women with PCOS, but in normal men and women as well [16-18, 22]. The results of these studies suggest hyperinsulinemia plays a central role in the pathogenesis of PCOS by decreasing the serum sex hormone binding globulin (SHBG) levels [22].

Sonographic parameters did not differ significantly between lean and obese PCOS women. In agreement with the observations of previous studies [19], we found a mean ovarian volume greater than the mean volume of a normal ovary, which has a volume of 6.8±2.4 ml, upper limit: 10.7 ml [21]. The fact that a portion of lean women had an ovarian volume <10.7 ml lessens the importance of ovarian size as an ultrasonographic diagnostic criterion of PCOS.

Mean follicle number per ovary was similar between the two groups. Lean and obese PCOS patients had values greater than 9, which is the upper limit of the follicle number per normal ovary [21]. It seems that a mean follicle number >9 is an important diagnostic criterion of PCOS. The mean endometrial thickness did not differ between the two groups, but the mean endometrial surface area in obese PCOS women (10.1±1.9 cm^2) was significantly greater than in lean PCOS women (7.6±2.2 cm^2).

The total stromal volume was not significantly different between lean and obese women, but it was greater than the total stromal volume of normal ovaries (~8.5 ml).

Detection of stromal hyperchogenicity on ultrasound is an important criterion for diagnosis, but the subjectivity of this parameter has hindered attempts to produce meaningful comparative analyses in PCOS. Computerized three-dimensional (3D) ultrasound systems help us, for the first time, to visualize the transverse plane of the pelvis and to make direct measurement of ovarian and stromal volume. The advantage of using a 3D ultrasound system lies in its ability to provide follicular measurements, which can be subtracted from the total volume to give a more accurate estimation of stromal volume.

Conclusion

It is concluded that lean and obese PCOS women do not differ significantly in terms of the sonographic parameters of ovarian morphology. 3D ultrasound systems will facilitate a more accurate ovarian morphology assessment and increase our ability to examine important structure-function relationships in the ovary. However the hormonal status was not identical in the two groups. Hyperinsulnemia and low SHBG levels characterize obese PCOS women and regulation of SHBG metabolism by insulin is a possible explanation.

References

[1] Dunaif A., Givens J. R., Haseltine F., Merrian G. R.: "The polycystic syndrome". Cambridge, Blackwell Scientific, 1992.

[2] Franks S., Medical Progress: "Polycystic ovary syndrome". *N. Engl. J. Med.*, 1995, *333*, 853.

[3] Ardaens Y., Fossati P., Robert Y., Dewailly D., Lemaitre L.: "Polycystic ovary disease: contribution of vaginal endosonography and reassessment of ultrasonic diagnosis". *Fertil. Steril.*, 1991, *55*, 1062.

[4] Puzigaca Z., Prelevic G. M., Stretenovic Z., Balint Peric L.: "Ovarian enlargement as a possible marker of androgen activity in polycystic ovary syndrome". *Gynecol. Endocrinol.*, 1991, *5*, 167.

[5] Adams J., Polson D. W., Abdulmalid N., Morris D. V., Franks S., Mason N. D.: "Multifollicular ovaries: clinical and endocrine features and response to pulsatile GnRH". *Lancet*, 1985, *2*, 1375.

[6] Robinson S., Kiddy D., Gelding S.: "Decreased insulin sensitivity in women with polycystic ovaries is related to menstrual disturbance". *Clin. Endocrinol.*, 1993, *39*, 368.

[7] Dunaif A., Mandeli I., Fluhr H., Dobrjansky A.: "The impact of obesity and chronic hyperinsulinemia on gonatropin release and gonadal steroid secretion in the polycystic ovary syndrome". *J. Clin. Endocrinol. Metab.*, 1988, *66*, 131.

[8] Singh K. B., Mahajan D. K., Wortsman J.: "Effect of obesity on the hormonal characteristics of the polycystic ovary syndrome". *J. Reproduct. Med. Obstet. Gynecol.*, 1994, *39*, 805.

[9] Zhang Y. W., Stern B., Rebar R. W.: "Endocrine comparison of obese menstruating and amenorrheic women". *J. Clin. Endocrin. Metab.*, 1984, *58*, 1077.

[10] Pasqualli R., Casimirri F.: "The impact of obesity on hyperadrogenism and polycystic ovary syndrome in premenopausal women". *Clin. Endocr.*, 1993, *39*, 1.

[11] Holte J., Bergh T.: "The independent effects of polycystic ovary syndrome and obesity on serum concentrations of gonadotropins and sex steroids in premenopausal women". *Clin. Endocr.*, 1994, *41*, 472.

[12] Kiddy D. S., Hamilton D., Bush A.: "Differences in clinical and endocrine features between obese and non-obese subjects with PCOS". *Clin. Endocr. (Oxf.)*, 1990, *32*, 213.

[13] Pasquali R., Antenucci, Casimirri F., Venturoli S., Paradisi R., Fabbri R. *et al.*: "Clinical and hormonal characteristics of obese women before and after weight loss". *J. Clin. Endocrinol. Metab.*, 1989, *68*, 173.

[14] Dunaif A., Graf M., Mandeli J., Laumas V., Dobrjansky A.: "Characterization of groups of hyperandrogenic women with acanthosis nigricans, impaired glucose tolerance, and/or hyperinsulinemia". *J. Clin. Endocrinol. Metab.*, 1987, *65*, 499.
[15] O'Meara N. M., Blackman J. D., Ehrmarn D. A., Barnes R. B., Jaspan J. B., Rosenfield R. L. *et al.*: "Defects in beta-cell function in functional ovarian hyperandrogenism". *J. Clin. Endocrinol. Metab.*, 1993, *76*, 1241.
[16] Peris A. N., Stagnor J. I., Plymate S. R.: "Relationship of insulin secretory pulses to sex hormone-binding globulin in normal men". *J. Clin. Endocr. Metab.*, 1993, *76*, 279.
[17] Preziosi D., Barret-Connor E., Dapoz L.: "Interrelation between plasma sex hormone-binding globulin and plasma insulin in healthy adult women. The Telecom Study". *J. Clin. Endocrinol. Metab.*, 1993, *76*, 283.
[18] Nestler J. E., Powers L. P., Matt D. W.: "A direct effect of hyperinsulinemia on serum SHBG levels in obese women with the polycystic ovary syndrome". *J. Clin. Endocr. Metab.*, 1991, *72*, 83.
[19] Swanson M., Sauerbrei E. E., Cooperberg P. L.: "Medical implications of ultrasonically detected polycystic ovaries". *J. Clin. Ultrasound*, 1981, *9*, 219.
[20] Orsini L., Venturoli S., Lorusso R.: "Ultrasonic findings in PCOS". *Fertil. Steril.*, 1985, *43*, 709.
[21] Van Santbrick J. P., Hop C., Fauser J. M.: "Classification of normogonadotropic infertility: polycystic ovaries diagnosed by ultrasound versus endocrine characteristics of PCOS". *Fert. Steril.*, 1977, *67*, 452.
[22] Nestler J. E., Powers L. P., Matt D. W., Steingold K. A., Plymate S. R., Rittmaster R. S. *et al.*: "A direct effect of hyperinsulinemia on serum-sex hormone-binding globulin levels in obese women with the polycystic ovary syndrome". *J. Clin. Endocrinol. Metab.*, 1991, *72*, 83.

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