ORIGINAL ARTICLE

https://doi.org/10.1590/1806-9282.20230874

Polycystic ovary syndrome and abdominal fat: is there a relationship?

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SUMMARY

OBJECTIVE: The aim of this study was to compare the distribution of fat tissue in non-obese women with polycystic ovary syndrome and those without the syndrome using dual-energy radiological densitometry.

METHODS: This was a case-control study in which we enrolled women aged 14–39 years with polycystic ovary syndrome according to the Rotterdam criteria with a body mass index between 18.5 and 30 kg/m^2. The control group comprised women with the same profile, but without polycystic ovary syndrome. Patients were treated at the Endocrinological Gynecology Outpatient Clinic of the Department of Obstetrics and Gynecology of the Irmandade da Santa Casa de Misericórdia de São Paulo between 2019 and 2022. Anthropometric measurements were taken and the assessment of body composition was performed using dual-energy radiological densitometry.

RESULTS: The sample comprised 57 women: 37 in the polycystic ovary syndrome group and 20 in the control group. The mean age of the polycystic ovary syndrome group was 24.9 years (±6.9) with a mean body mass index of 60.8 kg/m^2 (±8.5), and for the control group, it was 24.2 years (±6.9) with a mean body mass index of 58 kg/m^2 (±8.4). Body composition was evaluated using dual-energy radiological densitometry and showed a higher value of trunk fat in the polycystic ovary syndrome group (44.1%, ±9.0) compared to the control group (35.2%, ±11.4), which was statistically significant (p=0.002).

CONCLUSION: Our study showed that non-obese polycystic ovary syndrome patients have a higher concentration of abdominal fat, which is a risk factor for increased cardiovascular risk and insulin resistance.

ClinicalTrials.gov ID: NCT02467751.

KEYWORDS: Polycystic ovary syndrome. Body composition. Insulin resistance. Hyperandrogenism. Body mass index.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous clinical condition characterized by hirsutism, menstrual irregularity, infertility, and endocrine changes such as hyperandrogenism. Its prevalence may vary according to the criteria used for its diagnosis, and it ranges from 9 to 18%. Abdominal obesity is present in approximately 50% of women with PCOS, with onset in late childhood and increasing during puberty. The clinical phenotype and development of PCOS are enhanced by the presence of obesity, especially among those who are prone to genetic disorders[1].

Assessment of body composition by dual-energy radiological densitometry (DEXA) occurs when an X-ray or photon source is placed on one side of the object and the intensity of the beam on the opposite side is related to its thickness, density, and chemical composition. This attenuation phenomenon depends on the energy of the incident photon and is different in bone, lean mass, and fat tissue, reflecting their different densities and chemical composition[2]. DEXA measures visceral and subcutaneous fat accurately and reliably and is a technique that surpasses the accuracy of anthropometric measurements due to its precision in measuring body fat. The software used with DEXA calculates fat in different regions of the body[3]. It is a non-invasive technique that is easy to perform, safe, and low risk. Studies have shown strong correlations in the assessment of body fat with DEXA, indicating that the method can be considered as a reference for measuring adiposity in epidemiological studies. Anthropometric indices, such as body mass index (BMI) and waist circumference, remain the most used parameters to assess adiposity due to their simplicity; however, these indices do not directly measure the amount of adipose tissue and there is no distinction between fat and lean mass, so this raises questions about the validity of anthropometric measures[3-5].

The objective of this study was to compare the distribution of fat tissue using DEXA in non-obese women with PCOS compared to those without the syndrome.

METHODS

This was a case-control study in which we enrolled women aged between 14 and 39 years with PCOS according to the

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Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
Received on July 21, 2023. Accepted on July 27, 2023.

Rotterdam criteria[1], with a BMI between 18.5 and 30 kg/m^2 and who were not using contraceptives. The control group comprised women with the same profile but without PCOS. Patients were treated at the Endocrinological Gynecology Outpatient Clinic of the Department of Obstetrics and Gynecology of the Irmandade da Santa Casa de Misericórdia de São Paulo between 2019 and 2022.

The patients were in menacme and they answered questions about the menstrual cycle, acne, hirsutism, and medication use. Body weight (kg) was obtained using an electronic scale (accuracy of 0.1 kg) with an empty bladder and with the woman wearing only underwear. Height (m) was obtained using a wall stadiometer with the woman barefoot and with a precision of 0.5 cm. Thus, we calculated the BMI (BMI=weight/height^2) (kg/m^2), as recommended by the World Health Organization for assessing nutritional status[6]. To measure waist circumference (cm), the tape on the lesser curvature located between the last costal arch and the iliac crest. All anthropometric measurements were performed by a single researcher throughout the entire project.

Clinical hyperandrogenism was evaluated using the modified Ferriman-Gallwey index according to the criteria adopted by Hatch et al.[7], women with a score greater than eight being considered hirsute[8]. In both groups, we evaluated lipoprotein profile [total cholesterol and fractions (mg/dL)], triglycerides (TG) (mg/dL), insulin dosage (μIU/mL), fasting glucose (mg/dL), and classic glycemic curve (2 h) (mg/dL).

Laboratory hyperandrogenism was evaluated through measurements of total testosterone (testosterone T) (ng/dL), dehydroepiandrosterone (DHEA) (ng/dL), dehydroepiandrosterone sulfate (SDHEA) (μg/dL), 17 alpha-hydroxyprogesterone (17OHP) (ng/mL), and sex hormone binding globulin (SHBG) (nmol/L). The following were also measured: thyroid-stimulation hormone (TSH), free tetraiodothyronine (T4l), luteinizing hormone (LH) (mUI/mL), and follicle stimulating hormone (FSH) (mUI/mL).

Hormonal and insulin dosages were performed using the chemiluminescence method with an Immulite 2000 device. Hormonal tests were collected from all women who menstruated in the follicular phase between the third and fifth day. Blood collection occurred after a 12-h fast in the morning. FSH, LH, TSH, free T4, total testosterone, prolactin, classic glycemic curve, and insulin were evaluated by electrochemiluminescence, with a COBAS 6000-ROCHE device. 17OHP was determined by radioimmunoassay. DHEA, S-DHEA, and SHBG were analyzed by electrochemiluminescence in Roche Modular-cobas 601 automation.

Total cholesterol, serum concentrations of high-density lipoprotein, and TG were measured by the enzymatic method using the BT 3000 plus device (Wiener lab®, Rosario, Argentina). The low-density lipoprotein (LDL) value was calculated and obtained using the Friedewald formula (LDLc=TC-HDLc-TG/5)[9]. The homeostatic model for the assessment of insulin resistance (HOMA-IR) was calculated using the formula: {(fasting glucose in mg/dL´0.05551)´fasting insulin in μU/mL}/22.5[10]. All measurements were performed at the Central Laboratory of Santa Casa de São Paulo.

Transvaginal pelvic ultrasound was performed in all women, those menstruating during the follicular phase from the third to the fifth day of the cycle with the Voluson 730 expert machine (GE Medical Systems, ZIPF, Austria). The ovarian volume and the number/size of follicles present in these organs were evaluated. To calculate the ovarian volume, the prolate ellipsoid formula was used (depth´width´length´0.5)[11].

The diagnosis of PCOS was obtained using the Rotterdam criteria, which defines it in the presence of two of the following three criteria: oligomenorrhea or anovulation; clinical or laboratory hyperandrogenism; and ovaries with a polycystic appearance on ultrasound (20 or more follicles measuring between 2 and 9 mm in diameter or increased ovarian volume >10 cm^3). Other causes of menstrual irregularity and hyperandrogenism, such as hyperprolactinemia, hypothyroidism, Cushing's syndrome, non-classical forms of congenital adrenal hyperplasia, and androgen-secreting neoplasms, should also be excluded[1].

Inclusion criteria: PCOS group: Women with PCOS according to the Rotterdam criteria, with a BMI between 18.5 and <30 kg/m^2, and not using contraceptives. Control group: Women without PCOS, with a BMI between 18.5 and <30 kg/m^2, without contraceptive use, with regular cycles, and without medication in the past 3 months.

Exclusion criteria: Women with BMI between 18.5 and >30 kg/m^2, using oral contraceptives in 3 months prior to inclusion in the study, using corticosteroids, antiandrogenic drugs, statins, hyperprolactinemia, congenital adrenal hyperplasia, Cushing's syndrome, history of angina or myocardial infarction, thrombogenic diseases, hematological disease, systemic, vascular, or thyroid disease, infection or inflammation, malignant disease, patients with diabetes or medications that alter insulin resistance in the last 3 months, pregnant women, women with kidney or liver dysfunction, and alcoholics.

The assessment of body composition was performed using DEXA, which is an absorption technique of two low energy beams emitted by RX (DXA-dual x-ray-absorptiometry) in a densitometer of the brand LUNAR – GE of the whole body, being then obtained the corporal composition[12].

The study was approved by the hospital Ethics Committee number 167/10. The statistical tests used were Student's t-test and the Mann-Whitney U test with a significance level of 5%.

RESULTS

We initially selected 102 women who met the inclusion criteria, with 55 volunteers allocated to the PCOS group and 47 to the control group; however, in the PCOS group, 18 did not attend the exams, and in the control group, 27 did not attend (Figure 1). The final sample therefore comprised 57 participants, who were divided into two groups: 37 in the PCOS group and 20 in the control group. The mean age of the PCOS group was 24.9 years (SD ±6.9) with a BMI of 60.8 kg/m^2 (SD ±8.5) and the mean age of the control group was 24.2 years (SD ±6.9) with a BMI of 58 kg/m^2 (SD ±8.4), without any statistically significant differences between the groups (Table 1).

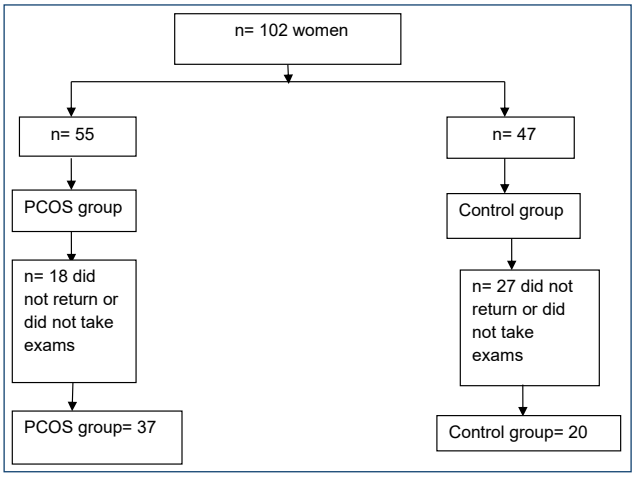

Figure 1. Patient selection flowchart.

There was a significant difference in the following studied parameters: fasting blood glucose (mg/dL) in the PCOS group (88.6±7.9) in relation to the control group (84.2±7.2) (p=0.045) and HOMA-IR in the PCOS group 1.8 (0.4–6.7) and the control group 1.4 (0.7–3.2) (p=0.034). The 2 h blood glucose (mg/dL) (p=0.146), glycated hemoglobin (%) (p=0.056), and insulin (µIU/mL) (p=0.086) had higher values in the PCOS group than in the control group. Total cholesterol (mg/dL), LDL (mg/dL), high-density lipoprotein (HDL) (mg/dL), and TG (mg/dL) did not show significant differences between the studied groups (Table 1).

Serum concentrations of the following analyzed items showed significant differences and were higher in the PCOS group: LH (mIU/mL) 5.4 (0.7–26.4) versus 4 (0.3–7.2) (p=0.026), 17 hydroxyprogesterone (ng/mL) 1.1 (±0.4) versus 0.7 (±0.4) (p=0.005), and total testosterone (ng/dL) 33 (20–109) versus 22.5 (20–55.8) (p=0.003). SHBG values (nmol/L) were higher in the control group than in the PCOS group 89.5 (34–159.8) versus 48.1 (13.3–360) (p=0.004). Serum concentrations of FSH (mIU/mL), DHEA (ng/dL), S-DHEA (µg/dL), and prolactin (ng/mL) were not significant (Table 2).

Body composition was evaluated using DEXA technique and there was a statistically significant (p=0.002) higher value of trunk fat in the PCOS group (44.1%, SD ±9.0) compared to the control group (35.2%, SD ±11.4) (Table 2).

Table 1. Anthropometric characteristics and biochemical parameters of women in the polycystic ovary syndrome group and in the control group.

Variable	PCOS group Median (range)	Control group Median (range)	p
Age (years)	24.9 (±6.9)	24.2 (±6.9)	0.728*
Weight (kg)	60.8 (±8.5)	58.0 (±8.4)	0.242*
BMI (kg/m^2)	23.1 (±3.1)	22.2 (±3.1)	0.311*
Total cholesterol (mg/L)[a]	160.6 (±34.4)	155.3 (±33.8)	0.580*
Low-density lipoprotein (mg/L)	98 (43–143)	90.5 (50–154)	0.694**
High-density lipoprotein (mg/L)	49 (31–115)	51 (36–90)	0.280**
TG (mg/L)	72 (34–173)	57 (35–109)	0.120**
Fasting glucose (mg/L)[a]	88.6 (±7.9)	84.2 (±7.2)	**0.045***
2 h blood glucose (mg/L)	98 (50–240)	89 (69–153)	0.146**
Glycated hemoglobin (%)	5.4 (4–6)	5.1 (5–6)	0.056**
Insulin (uIU/mL)	8.8 (1.9–34.3)	6.8 (3.8–14.4)	0.086**
HOMA-IR	1.8 (0.4–6.7)	1.4 (0.7–3.2)	**0.034****

BMI: body mass index. Statistically significant values are denoted in bold. *Student's t-test; **Mann-Whitney U test; [a]mean±SD; p<0.05.

Table 2. Hormonal parameters and comparison of body composition by in women in the polycystic ovary syndrome group and in the control group.

Variable	PCOS group Median (range)	Control group Median (range)	p
Follicle-stimulating hormone (mUI/mL)	4.3 (2–7.6)	5.6 (0.7–14.2)	0.242*
LH (mUI/mL)	5.4 (0.7–26.4)	4 (0.3–7.2)	**0.026***
17OHP (ng/mL)[a]	1.1 (±0.4)	0.7 (±0.4)	**0.005****
Total testosterone (ng/dL)	33 (20–109)	22.5 (20–55.8)	**0.003***
DHEA (ng/dL)	6.1 (2.1–13.9)	4.7 (1.1–37.1)	0.281*
SDHEA (ug/L)	296 (53–3670)	212.5 (39.3–1390)	0.422*
Prolactin (ng/mL)	10.7 (3.3–47.1)	10.5 (4.9–20)	0.631*
Sex hormone-binding globulin (nmol/L)	48.1 (13.3–360)	89.5 (34–159.8)	**0.004***
Body fat (%)	38.6 (13.3–48.6)	34.0 (16.1–53.4)	0.165*
Truncal fat (%)[a]	44.1 (±9.0)	35.2 (±11.4)	**0.002****
Leg fat (%)[a]	40.1 (±6.4)	37.4 (±9.3)	0.191**

Statistically significant values are denoted in bold. *Mann-Whitney U test; **Student's t-test; [a]mean±SD; p<0.05.

DISCUSSION

We selected women diagnosed with PCOS and with a BMI between 18.5 and <30 for our study. We were interested in this group, as women with PCOS are traditionally obese. However, recent studies have shown that several factors are involved in the pathophysiology of PCOS and that even women with normal or low weight can be carriers of the syndrome.[1]

One of the hallmarks of PCOS is an excess of androgens. In our study, we found an increase in LH, total testosterone, and 17OHP and a decrease in SHBG in the PCOS group, similar to other studies[3,4,5,13]. Increased androgen biosynthesis by the ovaries results in hypothalamic-pituitary-ovarian axis abnormalities. The increase in LH production and the synergistic action with insulin lead to increased androgen production in theca cells. Insulin has a molecular structure similar to insulin-like growth factors and binds to the insulin-like growth factor-1 (IGF-1) receptor, increasing the response of theca cells to LH and, consequently, increasing androgen production[13].

Another issue that caught our attention was the fact that there are controversies in the literature as to which is the best method for measuring the amount of abdominal, trunk, and extremity fat in this group of women. Different methods can be used to assess the amount and distribution of body fat[3,4,14].

In our study, we selected DEXA to assess the amount and distribution of fat. The main advantage of this method is that it allows the direct measurement of the amount of fat in different regions of the body and provides numerical data independent of the operator. In addition, it is a simple method that can be used in population studies. Its main disadvantage is that it is unable to differentiate between subcutaneous and visceral fat[3-5].

However, abdominal fat is metabolically active and linked to insulin resistance and early vascular changes, so the assessment of abdominal fat by DEXA is a good indicator of the metabolic and cardiovascular consequences of obesity and may be a better indicator than a simple determination of visceral fat[15].

In patient with PCOS, excess central fat has been associated with increased insulin resistance. A strong correlation has also been observed using abdominal ultrasound between levels of visceral fat and insulin resistance, as well as metabolic dysfunction[16,17]. In our study, DEXA showed that patients with PCOS had a statistically significant higher concentration of fat in the trunk than the volunteers in the control group.

CONCLUSION

Our study showed that non-obese PCOS patients had a statistically significant higher concentration of abdominal fat than the control group comprising volunteers without PCOS. Increased abdominal fat is probably related to increased cardiovascular risk and insulin resistance.

AUTHORS' CONTRIBUTIONS

CFM: Data curation, Formal Analysis, Funding acquisition, Investigation, Project administration, Resources, Software, Validation, Writing – original draft, Writing – review & editing. **SMRRL:** Conceptualization, Funding acquisition, Methodology, Resources, Supervision, Validation, Visualization.

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