

# Metabolic Syndrome in Women with Polycystic Ovary Syndrome: Prevalence, Characteristics and Predictors

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ABSTRACT

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The aim of this study was to determine the prevalence of metabolic syndrome in women with polycystic ovary syndrome, as well as its characteristics and predictors. Seventy-three women, with body mass index of  $30.4 \pm 7.8$  kg/m<sup>2</sup> and  $25.0 \pm 6.0$  years old, subdivided according to body mass index, were studied retrospectively. There was no significant mean age difference among body mass index groups ( $p = 0.228$ ). Prevalence of metabolic syndrome was 38.4%, with a null prevalence for normal ( $n = 18$ ), 23.8% for overweight ( $n = 17$ ), 62.9% for obese ( $n = 28$ ), and 85.5% for morbidly obese women ( $n = 7$ ). Women with metabolic syndrome were older than women without metabolic syndrome ( $27.3 \pm 5.3$  vs.  $24.2 \pm 4.6$  vs. years old;  $p = 0.031$ ) and presented a higher body mass index ( $36.3 \pm 7.7$  vs.  $26.9 \pm 5.4$ ;  $p < 0.001$ ). There was no difference for degree of hirsutism and menstrual patterns between women with and without metabolic syndrome ( $p = 0.593$  and  $p = 0.119$ , respectively). Regarding laboratory parameters, DHEAS was lower ( $1,646 \pm 1,007$  vs.  $2,594 \pm 1,563$ ;  $p = 0.007$ ) and HOMA-IR were higher ( $9.9 \pm 9.7$  vs.  $4.6 \pm 4.7$ ;  $p = 0.004$ ) in women with metabolic syndrome ( $p = 0.031$  and  $p < 0.001$ , respectively). The best predictors of metabolic syndrome were waist circumference  $> 88$  cm, HDL-cholesterol  $< 50$  mg/dL and triglycerides  $\geq 150$  mg/dL. (**Arq Bras Endocrinol Metab 2007;51/6:972-979**)

**Keywords:** Polycystic ovary syndrome; Metabolic syndrome; Insulin resistance; Cardiovascular risk

RESUMO

**Síndrome Metabólica em Mulheres com Síndrome dos Ovários Policísticos: Prevalência, Características e Preditores.**

O objetivo deste estudo foi o de determinar a prevalência, características e preditores da síndrome metabólica em mulheres com a síndrome dos ovários policísticos. Setenta e três mulheres, com índice de massa corporal de  $30,4 \pm 7,8$  kg/m<sup>2</sup> e  $25,0 \pm 6,0$  anos de idade, subdivididas de acordo com o índice de massa corporal, foram estudadas retrospectivamente. Não se observou diferença significativa de idade entre os grupos ( $p = 0,228$ ). A prevalência da síndrome metabólica foi de 38,4%, estando ausente nas mulheres com índice de massa corporal normal ( $n = 18$ ) e presente em 23,8% das com sobrepeso ( $n = 17$ ), 62,9% das obesas ( $n = 28$ ) e 85,5% das obesas mórbidas ( $n = 7$ ). Quando comparadas, as mulheres com síndrome metabólica apresentaram uma idade mais avançada ( $27,3 \pm 5,3$  vs.  $24,2 \pm 4,6$  anos;  $p = 0,031$ ) e um índice de massa corporal maior ( $36,3 \pm 7,7$  vs.  $26,9 \pm 5,4$ ;  $p < 0,001$ ) que as mulheres sem a síndrome, não havendo diferença significativa com relação ao grau de hirsutismo ( $p = 0,593$ ) e padrão menstrual ( $p = 0,119$ ). Com relação aos parâmetros laboratoriais, a concentração de DHEAS foi menor ( $1.646 \pm 1.007$  vs.  $2.594 \pm 1.563$ ;  $p = 0,007$ ) e o valor do HOMA-IR foi maior ( $9,9 \pm 9,7$  vs.  $4,6 \pm 4,7$ ;  $p = 0,004$ ) nas pacientes com a síndrome metabólica. Os melhores preditores para a presença da síndrome metabólica foram a circunferência abdominal  $> 88$  cm, HDL-colesterol  $< 50$  mg/dL e triglicérides  $\geq 150$  mg/dL. (**Arq Bras Endocrinol Metab 2007;51/6:972-979**)

**Descritores:** Síndrome dos ovários policísticos; Síndrome metabólica; Resistência à insulina; Risco cardiovascular

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**P**OLYCYSTIC OVARY SYNDROME (PCOS) is a heterogeneous disorder, characterized by chronic anovulation and hyperandrogenism. It affects between 5 to 10% of women of reproductive age, and it is considered one of the most common endocrine disorders in premenopausal women (1).

Since the study by Burghen et al. (2), in 1980, which reported that women with PCOS had basal and glucose-stimulated hyperinsulinemia, suggesting the presence of insulin resistance, it has become clear that the syndrome also has a component of metabolic disorder, beyond reproductive morbidities. In fact, Dalghren et al. (3), in 1992, reported that the prevalence of diabetes mellitus in menopausal women with previous PCOS was higher than that observed in the general population, 15% versus 2.3%. Furthermore, insulin resistance (4), dyslipidemia (5,6), central obesity (7), and hypertension (8,9) started to be commonly described as being associated with PCOS. Nowadays, PCOS is considered a complex metabolic disorder and a risk factor for diabetes mellitus and cardiovascular disease. It is considered that insulin resistance can be a link between carbohydrate intolerance and the increase in cardiovascular risk and PCOS (10) and that insulin resistance also plays a pathogenic role in the metabolic syndrome (11). Furthermore, cardiovascular and diabetes mellitus type 2 risk factors defining metabolic syndrome are prevalent in PCOS (5-9,12).

The data regarding the prevalence of metabolic syndrome in PCOS are scarce, and limited only to the USA (13-17) and Europe (18-20). In the USA population, its prevalence in adolescents was 37% (14), while in adult women it varied from 34.4% (16) to 47.9% (17). In Southern Italy its prevalence was 8.2% (20) and 8.4 to 16% in Turkey (19), while Czech women with polycystic ovary syndrome were rarely described, although its isolated features were relatively frequent (18).

This study aimed at analyzing the prevalence, characteristics and predictors of metabolic syndrome in women with PCOS from a single University Hospital from the city of São Paulo, Brazil.

## SUBJECTS AND METHODS

The study protocol, as a retrospective study, was approved by the Ethical Committee of the Hospital das Clínicas da Universidade de São Paulo.

### Subjects

All women who were seen in the Outpatient Clinic (Endocrine Unit and Gynecology Unit) of Hospital das Clínicas of São Paulo from 1995 to 2004 were initially included in the study.

The women were referred to the clinic for hirsutism evaluation. All of them came from the urban area of the city of São Paulo; regarding ethnicity, most were Caucasian and Brazilian mulatto and none of them were Black. Diagnosis of PCOS was based on the presence of hirsutism and/or hyperandrogenemia and menstrual dysfunction, after exclusion of Cushing's syndrome, late-onset 21-hydroxylase deficiency, thyroid dysfunction, hyperprolactinemia, or androgen-secreting tumor by appropriated tests, according to the 1990 National Institute of Child Health and Women Development (21). None of the patients had other diseases or were taking any medication for at least 6 months prior to the study.

A modified National Cholesterol Education Program Adult Treatment Panel (NCET ATP III) criteria (22), as suggested by the Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (23), which also included glycemia at the OGTT, together with fasting glycemia as a single criteria, was used for the diagnosis of metabolic syndrome, by the presence of three or more of the following abnormalities: waist circumference > 88 cm; fasting glucose  $\geq$  110 mg/dL and/or glycemia at the 120 minutes of the oral glucose tolerance test  $\geq$  140 mg/dL; fasting serum triglycerides  $\geq$  150 mg/dL, serum HDL-C < 50 mg/dL and blood pressure  $\geq$  130/85 mmHg. Only women who had the complete panel of clinical and laboratory data for the classification of PCOS and metabolic syndrome were included in the final analysis.

Blood pressure (BP) was measured with a mercury sphygmomanometer with rubber sleeves of different sizes, according to the women's arm circumference. The women stayed in supine position after a 20-minute resting period. The systolic (SBP) and diastolic (DBP) pressures were measured twice on average. We considered hypertension a blood pressure level equal or higher than 130 mmHg for SBP and 85 mmHg for DBP, in accordance with the Brazilian Guidelines in Arterial Hypertension (24).

Body mass index (BMI) was calculated with the formula: weight (kg)/height (m<sup>2</sup>).

Waist circumference was measured with the patient lying down, at the level of the umbilicus.

Hirsutism was defined by the presence of excessive body hair distributed in an androgen-depend pattern, using the Ferriman & Gallwey score > 8 (25).

Eumenorrhea was defined as the presence of menstrual cycles between 25 and 34 days. At least two consecutive cycles with low progesterone levels (< 3 ng/mL) were required for a diagnosis of anovulation. Oligomenorrhea was defined as the presence of three or more cycles of > 35 days in the previous 6 months and amenorrhea due to the lack of vaginal bleeding for 3 months. Hypermenorrhea was defined as the presence of vaginal bleeding at intervals < 21 days.

The women were subdivided in groups, according to BMI (normal: 18.5 to 24.9 kg/m<sup>2</sup>, overweight: 25.0 to 29.9 kg/m<sup>2</sup>, obese:  $\geq$  30 kg/m<sup>2</sup>, and morbidly obese:  $\geq$  40 kg/m<sup>2</sup>) and the presence of metabolic syndrome.

Insulin resistance was measured through the homeostatic model assessment (HOMA-IR), calculated as follows: fasting glucose (mmol/L) x fasting insulin ( $\mu$ UI/mL)/22.5.

Oral glucose tolerance test (OGTT) was performed between 7:30 and 8:30 A.M. After an overnight fast, blood samples were obtained through an IV catheter placed in the forearm for the determination of fasting blood glucose, insulin, gonadotropins (LH and FSH), estradiol ( $E_2$ ), total testosterone (testo) and dehydroepiandrosterone sulphate (DHEAS), triglycerides, and total cholesterol and its fractions (LDL-C and HDL-C). A 75-gr of glucose load was given, and blood was collected after 30, 60, 90, and 120 minutes thereafter, for determination of glucose and insulin. Samples were considered only when progesterone concentration at the basal sample was less than 1.0 ng/mL.

The states of glucose tolerance were classified according to the World Health Organization (WHO) (26) — impaired fasting glucose IFG: fasting plasma glucose  $\geq 110$  mg/dL and  $< 126$  mg/dL; impaired glucose tolerance: plasma glucose at 120 minutes  $\geq 140$  mg/dL and  $< 200$  mg/dL; diabetes: fasting plasma glucose  $\geq 126$  mg/dL and/or plasma glucose at 120 minutes  $\geq 200$  mg/dL.

## Methods

Plasma glucose concentration was determined by a glucose oxidase method.

All lipid determinations were measured directly in plasma samples. Plasma total cholesterol and triglycerides were determined using enzymatic methods (Roche Laboratories). HDL-C was measured by the same method as for cholesterol and LDL-C, which were estimated by the Friedewald formula.

For hormone assays, blood samples were processed by centrifuging, and serum was stored at  $-20$  °C until assayed.

Progesterone and testosterone were measured by fluoroimmunoassay (Wallac, Finland), insulin, LH and FSH were measured by immunofluorometric assay (Wallac, Finland) and DHEAS were measured by radioimmunoassay (Cisbio International, France, and DSL, Texas, USA).

All assays were performed in duplicate and the intraassay and interassay coefficients of variation did not exceed 10% and 15%, respectively.

## Statistical analysis

Descriptive statistics were calculated in order to present the results, mean and standard deviation.

Levine test was used to compare the group's variances. Mann-Whitney non-parametric test — U statistics — was used for group's comparison of means. This statistical analysis does not assume either normal distribution or homogeneity of variances. Chi-square test was used to test categorical or nominal variables association. Fisher's test was used in transformed variables (log) to evaluate Body Mass Index groups' effect. Performance measures were calculated (Predictive Positive Value, Predictive Negative Value, specificity, sensitivity, overall accuracy and Youden's Index) for metabolic syndrome characteristics.

The significance level used was 5%.

## RESULTS

Seventy-three women were included in the study, with BMI of  $30.4 \pm 7.8$  kg/m<sup>2</sup> and  $25.0 \pm 6.0$  years old. According to BMI, 24.7% were normal, 28.8% were overweight, 37.0% were obese and 9.6% were morbidly obese. There was no significant mean age difference among BMI groups ( $p = 0.228$ ). Except for 4 women with eumenorrhea and anovulatory cycles (5.5%), all of them presented menstrual abnormalities (5 with hypermenorrhea — 6.8%, 33 with oligomenorrhea — 45.2% and 31 with amenorrhea — 42.5%). Hirsutism was present in 83.8% of the women.

### Prevalence of the metabolic syndrome

Overall, the prevalence of metabolic syndrome according to the modified NCET ATP III was 38.4%. If the original criteria were considered, the prevalence of metabolic syndrome would be 28.8%, with a null prevalence for a BMI  $< 24.9$  kg/m<sup>2</sup> and increasing progressively according to the BMI (figure 1).

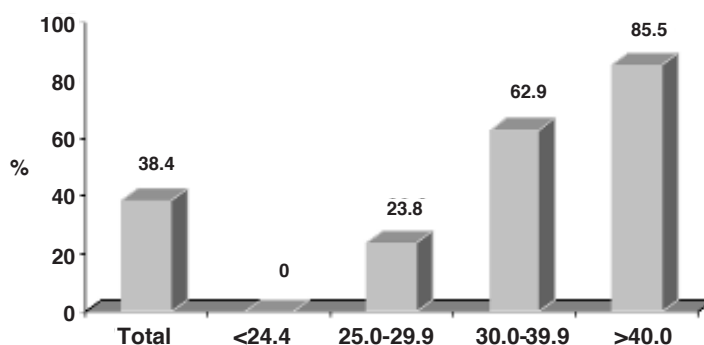
### Prevalence of each component of the metabolic syndrome

The prevalence of each criteria of metabolic syndrome in the whole group as well as stratified by BMI can be seen in table 1. Considering all women, the prevalence of one or no factor was observed in 43.9% of the women, and the prevalence of 3 or more factors was seen in 38.4% of them. Except for glucose at 120 minutes of the OGTT, there was a progressive increase in the prevalence of each criterion with the increase in BMI, with a decline for HDL-C  $< 50$  mg/dL and triglycerides  $\geq 150$  mg/dL for a BMI  $> 40$  kg/m<sup>2</sup>.

### Comparison between women with and without the metabolic syndrome

There was no difference between the menstrual pattern and degree of hirsutism between women with and without metabolic syndrome ( $p = 0.593$  and  $p = 0.119$ , respectively). As shown in table 2, women with the metabolic syndrome were older than women without it ( $p = 0.031$ ) and presented a higher BMI ( $p < 0.001$ ). Regarding the hormonal profile, only DHEAS was different between the groups, being lower in women with the metabolic syndrome ( $p = 0.007$ ).

As for the lipid profile, one woman who presented a concentration of triglycerides  $> 400$  mg/dL was eliminated from the comparison regarding the lipid profile. Total cholesterol and triglycerides were higher ( $p = 0.010$  and  $p < 0.001$ , respectively) and HDLC was lower ( $p < 0.001$ ) in women with the



**Figure 1.** Prevalence of metabolic syndrome stratified by body mass index in women with polycystic ovary syndrome.

**Table 1.** Prevalence (%) of individual characteristics of the metabolic syndrome among 73 patients with polycystic ovary syndrome stratified by body mass index.

| Characteristics                           | Total<br>(n = 73) | No MS*<br>(n = 45) | With MS<br>(n = 28) | Body mass index (Kg/m <sup>2</sup> ) |                       |                       |                 |
|---|-------------------|--------------------|---------------------|--------------------------------------|-----------------------|-----------------------|-----------------|
|   |                   |                    |                     | < 25.0<br>(n = 18)                   | 25.0-29.9<br>(n = 21) | 30.0-39.9<br>(n = 27) | ≥ 40<br>(n = 7) |
| Waist circumference > 88cm                | 49.3              | 26.7               | 87.5                | 0                                    | 33.3                  | 81.5                  | 100.0           |
| HDL-Cholesterol < 50 mg/dL                | 67.6              | 50.0               | 92.9                | 38.5                                 | 61.9                  | 85.2                  | 71.4            |
| Triglycerides ≥ 150 mg/dL                 | 31.8              | 7.7                | 66.7                | 0                                    | 30.0                  | 46.2                  | 42.9            |
| 130 SBP ≥ 130mmHg or DBP ≥ 85 mmHg**      | 24.7              | 8.9                | 50.0                | 5.6                                  | 9.5                   | 29.6                  | 100.0           |
| Fasting glucose ≥ 110 mg/dL               | 6.9               | 0                  | 47.9                | 0                                    | 4.8                   | 7.4                   | 28.6            |
| Glucose at 120 min of OGTT*** ≥ 140 mg/dL | 37.6              | 23.5               | 60.9                | 46.2                                 | 23.5                  | 45.5                  | 40.0            |

\* MS: metabolic syndrome; \*\* SBP: systolic blood pressure, DBP: diastolic blood pressure, \*\*\* OGTT: oral glucose tolerance test.

**Table 2.** Anthropometrics and laboratory data of women with polycystic ovary syndrome according to the presence of metabolic syndrome.

|                                      | Metabolic syndrome |               | p       |
|--------------------------------------|--------------------|---------------|---------|
|                                      | No                 | Yes           |         |
| Age (Years)                          | 24.2 ± 4.6         | 27.3 ± 5.3    | 0.031   |
| Body mass index (kg/m <sup>2</sup> ) | 26.9 ± 5.4         | 36.3 ± 7.7    | < 0.001 |
| Waist circumference (cm)             | 83.4 ± 12.1        | 102.8 ± 13.4  | < 0.001 |
| FSH (UI/L)                           | 5.1 ± 2.1          | 4.7 ± 1.7     | 0.296   |
| LH (UI/L)                            | 12.4 ± 7.4         | 8.9 ± 3.6     | 0.070   |
| Estradiol (pg/mL)                    | 78.3 ± 60.6        | 57.0 ± 25.5   | 0.196   |
| Testosterone (ng/dL)                 | 119.8 ± 46.6       | 105.7 ± 45.5  | 0.301   |
| DHEAS (ng/mL)                        | 2,594 ± 1,563      | 1,646 ± 1,007 | 0.007   |
| Glycemia (µg/dL)                     | 87.4 ± 9.2         | 100.4 ± 33.0  | 0.031   |
| Insulin (mUI/mL)                     | 19.1 ± 17.9        | 37.8 ± 37.4   | < 0.001 |
| HOMA-IR                              | 4.6 ± 4.7          | 9.9 ± 9.7     | 0.004   |
| Cholesterol (mg/dL)                  | 177.0 ± 30.8       | 192.2 ± 26.7  | 0.010   |
| Triglycerides (mg/dL)                | 97.4 ± 38.5        | 219.4 ± 209.6 | < 0.001 |
| LDL-Cholesterol (mg/dL)              | 109.7 ± 24.9       | 116.5 ± 25.4  | 0.161   |
| HDL-Cholesterol (mg/dL)              | 51.8 ± 15.4        | 37.5 ± 6.7    | < 0.001 |
| SBP mmHg                             | 11.8 ± 1.1         | 13.2 ± 1.7    | < 0.001 |
| DBP mmHg                             | 7.4 ± 1.0          | 8.5 ± 1.0     | < 0.001 |

LH: luteinizing hormone, FSH: follicle stimulating hormone, DHEAS: dehydroepiandrosterone sulphate, HOMA-IR: insulin resistance homeostatic model assessment, SBP: systolic blood pressure, DBP: diastolic blood pressure.

metabolic syndrome, while LDL-C did not show any difference between the groups.

The fasting glucose, insulin and HOMA-IR were higher in women with the metabolic syndrome ( $p = 0.031$ ,  $p < 0.001$ , and  $p = 0.004$ , respectively) and, as expected, as these were inclusion criteria, women with the metabolic syndrome presented higher waist circumference ( $p < 0.001$ ), systolic and diastolic blood pressures ( $p < 0.001$  for both).

**Prevalence of glucose intolerance**

According to the WHO criteria, when women without the metabolic syndrome were considered, none of them presented fasting glycemia  $\geq 110$  mg/dl. At the OGTT, 15.5% had impaired glucose tolerance and 2.2% had diabetes. On the other hand, regarding the women with the metabolic syndrome, 13 (46.4%) women presented impaired glucose tolerance (3 on basal glucose and 10 at OGTT) and 6 (21.4%) had diabetes (2 on basal glucose – 140 and 147 mg/dL, and 4 at OGTT).

**Performance measures for the metabolic syndrome characteristics**

The positive (the percentage of women who have the metabolic syndrome) and negative predictive (the percentage of women who do not have the metabolic syndrome) values for the individual component of the metabolic syndrome, as well as the sensitivity, specificity and the Youden’s Index, are shown in table 3. According to this Index, the best indicators of the metabolic syndrome were a waist circumference  $> 88$  cm, an HDL-C  $< 50$  mg/dL and triglycerides  $\geq 150$  mg/dL, with Indexes of 59, 59 and 58. For instance, while fasting glicemia  $\geq 110$  mg/dL was the best positive predictive value, with a sensitivity of 100% (all women with a basal glucose  $\geq 110$  mg/dL presented

the metabolic syndrome), it had a low negative predictive value, with a specificity of 28% (66.2% of the women with a basal glucose  $< 110$  mg/dL did not have the metabolic syndrome), with a Younde’s Index of 28.0. On the other hand, the Younde’s Index for a HDL-C  $< 50$  mg/dL was 59, with the lowest positive predictive value (56.5% of the women with a HDL-C  $< 50$  mg/dL presented the metabolic syndrome), but with the highest negative predict value (93% of the women with a HDL-C  $> 50$  mg/dL did not have the metabolic syndrome).

**DISCUSSION**

The metabolic syndrome and the polycystic ovary syndrome share some characteristics, such as a high rate of impaired glucose tolerance and risk factors for cardiovascular disease.

We employed a modification of the NCET APT III guidelines, as suggested by the Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group for the diagnosis of metabolic syndrome, which included glycemia at 120 minutes of the OGTT together with fasting glycemia as a single criterion (23). According to Legro et al. (27) and based on our own experience (12), these modified guidelines will identify more women with abnormal glucose tolerance. This is particularly true for women with PCOS and normal BMI, as it has been shown that the prevalence increases 6.7 times when the American Diabetes Association criteria (28) are employed *versus* the WHO criteria for the diagnosis of glucose intolerance in women with PCOS. According to this, the prevalence of metabolic syndrome by NCET ATP III guidelines was 28.8%, increasing to 38.8% when the modified guidelines were used.

**Table 3.** Performance measures for metabolic syndrome characteristics.

|   | PPV*  | PNV** | Specificity | Sensitivity | Overall Accuracy | Youden’s Index |
|---|-------|-------|-------------|-------------|------------------|----------------|
| Waist circumference $> 88$ cm                   | 66.7  | 89.2  | 86.0        | 73.0        | 78.0             | 59.0           |
| HDL-Cholesterol $< 50$ mg/dL                    | 56.5  | 92.6  | 93.0        | 66.0        | 77.0             | 59.0           |
| Triglycerides $\geq 150$ mg/dL                  | 85.7  | 80.7  | 64.0        | 93.0        | 82.0             | 58.0           |
| SBP $\geq 130$ mmHg or DBP $\geq 85$ mmHg***    | 77.8  | 74.5  | 50.0        | 91.0        | 75.0             | 41.0           |
| Fasting glucose $\geq 110$ mg/dL                | 100.0 | 66.2  | 28.0        | 100.0       | 79.0             | 28.0           |
| Glucose at 120 min of OGTT**** $\geq 140$ mg/dL | 63.6  | 72.5  | 50.0        | 82.0        | 70.0             | 32.0           |

\* Predictive Positive Value; \*\* Predictive Negative Value; \*\*\* SBP: systolic blood pressure and DBP: diastolic blood pressure; \*\*\*\*OGTT: oral glucose tolerance test

It is difficult to compare our data about prevalence of metabolic syndrome with that of metabolic syndrome in Brazil. The only data regarding its prevalence in Brazil comes from the semi-arid rural area of the Northeast region, in a predominantly Brazilian Mulatto and Black women population with more advanced age (29). Crude prevalence was 30.0%, while the age-adjusted prevalence was 24.8%. However, when the age younger than 45 years old was considered, the prevalence decreased to 18.2%. Our study population consisted of individuals who were predominantly Caucasian and Brazilian Mulatto, younger and that came from an urban area of the southwest region of Brazil, with different dietary habits. Nonetheless, our prevalence was higher than that observed in women younger than 45 years old.

The prevalence of metabolic syndrome found by us was similar to that found in adult or adolescent women with PCOS in the USA, i.e., 33.4% to 43%, which is 2-fold higher than the age-adjusted prevalence rate based on the NHANES III survey (30). In the USA, the prevalence of metabolic syndrome in adolescent girls was 37% (14) compared to 5% of NHANES III girls. Among adult women, the prevalence rates vary from 34% (17) to 47.3% (16), and these prevalence rates of metabolic syndrome under the age of 40 were comparable to the 44% rate reported for women aged 60–69 in the general US population. On the other hand, a lower prevalence was observed in Europe, being 1.6% in the Czech Republic (18), 2.3% in Turkey (19), and 8.2% to 16% in southern Italy (20).

Different criteria for PCOS and metabolic syndrome, as well as the characteristics of the population studied, such as age and BMI, could in part explain this discrepancy in the prevalence of MS in women with PCOS. Carmina et al. (20) subdivided their patients with PCOS into two subgroups, according to their particular phenotype, hyperandrogenism and chronic anovulation, compatible with the NIH criteria (21) and hyperandrogenism and polycystic ovaries, but normal ovulatory cycles, compatible with the Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group criteria (23). The prevalence decreases from 8.9% to 5.0%, according to the NCEP APT III criteria for metabolic syndrome (22), and from 17.3% to 10.6%, according to the WHO criteria (30).

In this study, women with PCOS and metabolic syndrome were more obese and older than women with PCOS without metabolic syndrome. Similarly, we observed that the prevalence of metabolic syndrome increased with age and BMI. An effect of age

alone could be discarded as an explanation for the differences between prevalence rates of metabolic syndrome, as a high prevalence of metabolic syndrome, of 37%, was found even in adolescent girls with PCOS. However, age could be an adjunct factor in precipitating metabolic syndrome, as its prevalence, after stratified by BMI, increase with age in PCOS women (17).

On the other hand, we observed a significant impact of BMI on the prevalence of metabolic syndrome in our patients with PCOS, being absent in women with normal BMI, and present in 23.8% of overweight, 62.9% of obese and 85.7% of morbidly obese women. Possibly, the prevalence of obesity and the impact of age could be the main determinant of the prevalence of metabolic syndrome in different populations. This could explain the higher prevalence in the USA (34.0% to 47.3%) (16,17) when compared to European women with PCOS (1.6 to 17.3%) (18–20). The adult USA patients with PCOS were older (from 18 to 39 years) and more obese (at least, 55% of them presented a BMI > 30 kg/m<sup>2</sup>), while in Europe, the age range varies from 22 to 28 and obesity was much less prevalent (less than 26%). In fact, in Czech women with PCOS, aged younger than 28 years and with BMI < 27 kg/m<sup>2</sup>, the prevalence of MS was the least observed (1.6% vs. 0 in the control group) (18). The only author that observed the presence of metabolic syndrome in lean women with PCOS was Carmina et al. (20), with a prevalence of 1.9% to 2.9%, according to the criteria for metabolic syndrome MS (NCAP ATP III and WHO, respectively).

We did not find any phenotypic differences between our patients with and without metabolic syndrome, considering menstrual patterns and degree of hirsutism. The same occurred regarding hormonal profile, except for DHEAS, which was lower in women with metabolic syndrome. Although total testosterone was not different in the other studies either, free testosterone was always high (15,17). In the study by Erhmann et al. (17), there was an increase in the prevalence of metabolic syndrome from the lowest to the highest quartile of free testosterone, which does not remain significant after adjusting for BMI. Regarding the lower level of DHEAS in women with metabolic syndrome, an inverse relationship between insulin and DHEAS in PCOS women has been previously demonstrated (32,33).

Considering the individual components of the metabolic syndrome, we observed that its prevalence increased with BMI. The prevalence of one or no factors was seen in 94.5% of our women with a BMI < 25 kg/m<sup>2</sup> and in none of the morbidly obese women,

while the prevalence of three or more factors was not seen in women with a BMI < 25 kg/m<sup>2</sup>, being present in 85.8% of the morbidly obese ones. The most frequent found abnormality was a HDL-C < 50 mg/dL in 67.6% of the women, followed by a waist circumference > 88 cm in 49.3% and triglyceride ≥ 150 mg/dL in 31.8%. High blood pressure and fasting plasma glucose was less frequently found (24.7% and 6.9%, respectively). This prevalence was not different from that found by Erhmann et al. (17) and Apridonidze et al. (15), except for a higher HDL-C, the second more prevalent component observed by these two authors. Nevertheless, the most common aggregates of variables were indexes of adiposity (obesity or waist circumference and a HDL-C < 50 mg/dL). Even in Czech women with PCOS, in whom the prevalence of metabolic syndrome was low (18), their isolated features were relatively frequent. It is noteworthy that the prevalence of the components of the metabolic syndrome increases with the BMI. The prevalence of one or no factors was seen in 94.5% of our patients with a BMI < 25 kg/m<sup>2</sup> and in none of the morbidly obese women, while the prevalence of three or more factors was not seen in women with a BMI < 25 kg/m<sup>2</sup>, being present in 85.8% of the morbidly obese ones.

Each component was evaluated for its value to either confirm or exclude the metabolic syndrome, and an index (the Youden's Index), based on specificity and sensitivity of each component, was calculated. The best Positive Predictive Value was basal glucose, as all women with a value > 110 mg/dL had the metabolic syndrome, but it identified only 28% of the women with MS. On the other hand, 92.6% of the women with a value of HDL-C > 50 mg/dL did not have the syndrome (Negative Predictive Value), although a value < 50 mg/dL was presented only by 56.5% of the women (Positive Predictive Value). According to the Youden's Index, the best predictors for metabolic syndrome was a WC > 88 cm, a HDL-C < 50 mg/dL and Triglycerides > 150 mg/dL, whereas the worst were basal and post-glucose concentrations. These data are in accordance with those from Erhmann et al. (17), as, although isolated, the best predictor for this author was a high level of triglycerides, with a PPV and a NPV of 83% and 90%, respectively.

In conclusion, we observed a high prevalence of metabolic syndrome in our patients with PCOS, which increased when glycemia at 120 minutes of the OGTT was included in the ATP III guidelines; we also observed that BMI has a significant impact on the prevalence of all individual components. In view of our results, we suggest that the assessment of metabolic

syndrome should be carried out in all overweight and obese women with PCOS. The best predictors of the metabolic syndrome were waist circumference, HDL-C, and triglycerides.

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