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ORIGINAL ARTICLE

# Obesity and polycystic ovary syndrome: association with cardiovascular risk factors in women of reproductive age

# Obesidade e síndrome dos ovários policísticos: associação com fatores de risco cardiovascular em mulheres em idade reprodutiva

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## ABSTRACT

**Objective:** Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder with a heterogeneous presentation, affecting 9–18% of reproductive-age women. Evidence indicates a higher risk of comorbidities in this group. This study assessed whether obesity in women with PCOS is linked to a greater prevalence of cardiovascular risk factors. **Methods:** A cross-sectional study was conducted with 107 women diagnosed with PCOS between 2019 and 2021. Participants were classified as obese or non-obese based on body mass index (BMI) and underwent anthropometric and laboratory evaluations. Comorbidities were assessed through HDL, LDL, triglycerides, fasting glucose, oral glucose tolerance test (OGTT), and blood pressure. Descriptive statistics used absolute and relative frequencies. Poisson regression with robust variance estimated prevalence ratios (PR) and 95% confidence intervals (CI) for metabolic syndrome, dyslipidemia, glucose intolerance, and blood pressure alterations. Obesity was the exposure variable ($p< 0.05$). **Results:** The mean age was 27 years; 47.7% were obese. Obese women had higher PRs for metabolic syndrome (PR=3.28; CI 95%: 1.72–6.27), dyslipidemia (PR=1.28; CI 95%: 1.04–1.58), glucose intolerance (PR=3.05; CI 95%: 1.40–6.62), and blood pressure changes. **Conclusion:** Obesity in women with PCOS is associated with a greater prevalence of comorbidities that increase cardiovascular risk.

**Keywords:** Polycystic Ovary Syndrome. Metabolic Syndrome. Obesity.

## RESUMO

**Objetivo:** Síndrome dos Ovários Policísticos (SOP) é um distúrbio endócrino comum, com apresentação heterogênea, que afeta de 9 a 18% das mulheres em idade reprodutiva. Evidências apontam maior risco de comorbidades nesse grupo. Este estudo investigou se a obesidade em mulheres com SOP está associada a maior prevalência de fatores de risco cardiovascular. **Métodos:** Estudo transversal com 107 mulheres diagnosticadas com SOP entre 2019 e 2021. As participantes foram classificadas como obesas ou não obesas com base no índice de massa corporal (IMC) e submetidas a avaliações antropométricas e laboratoriais. As comorbidades foram analisadas por meio de HDL, LDL, triglicerídeos, glicemia de jejum, teste oral de tolerância à glicose (TOTG) e pressão arterial. Utilizou-se estatística descritiva em frequências absolutas e relativas. A regressão de Poisson com variância robusta estimou razões de prevalência (RP) e intervalos de confiança de 95% (IC) para síndrome metabólica, dislipidemia, intolerância à glicose e alterações pressóricas, tendo obesidade como variável de exposição ($P < 0,05$). **Resultados:** A média de idade foi 27 anos; 47,7% eram obesas. Mulheres obesas apresentaram RPs mais elevadas para todas as comorbidades avaliadas. **Conclusão:** A obesidade em mulheres com SOP está associada a maior prevalência de condições que aumentam o risco cardiovascular.

**Palavras-chave:** Síndrome do Ovário Policístico. Síndrome Metabólica. Obesidade.

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## INTRODUCTION

Polycystic ovary syndrome (PCOS) is a multifactorial endocrine disorder characterized by chronic anovulation, hyperandrogenism, and metabolic abnormalities. The diagnosis is based on the Rotterdam criteria, which include oligomenorrhea or amenorrhea, clinical or biochemical signs of hyperandrogenism, or elevated antimüllerian hormone levels in adults, and polycystic ovarian morphology.[1,2] The prevalence of PCOS ranges from 9% to 18% in women of reproductive age.[2] Genetic predisposition and environmental factors, such as poor dietary habits and sedentary lifestyles, contribute to its phenotypic expression.[3-5]

Recent studies suggest that PCOS is associated with an increased risk of metabolic disturbances, including insulin resistance, in 50–70% of affected women.[4,6] This reduced insulin sensitivity may be linked to a higher prevalence of comorbidities, such as diabetes, metabolic syndrome, and dyslipidemia.[7,8] However, whether these comorbidities are more prevalent in obese women with PCOS remains controversial.[9] In Brazil, the prevalence of obesity among women with PCOS varies widely, reaching 30–60% in some studies.[10] Among adolescents, this figure can range from 40% to 70% in PCOS.[11]

A meta-analysis comparing the prevalence of metabolic disorders in non-obese women with and without PCOS concluded that women with PCOS have a higher likelihood of developing type 2 diabetes and alterations in glycemic and lipid profiles.[12] Thus, PCOS itself may be associated with an increased risk of cardiometabolic diseases owing to the combination of hormonal and metabolic abnormalities that promote dyslipidemia, insulin resistance, elevated blood pressure, and metabolic syndrome (MS).[13,14]

The prevalence of MS and other comorbidities in women with PCOS may vary depending on their lifestyle, ethnicity, geographic region, and dietary habits.[15,16] In Brazil, the prevalence of MS ranged from 24 to 42%; however, few studies have evaluated whether obesity increases the prevalence of comorbidities in Brazilian women with PCOS.[10]

This study aimed to assess the frequency of metabolic syndrome, dyslipidemia, impaired glucose tolerance, and altered blood pressure in women with PCOS, and to evaluate whether obese women with PCOS exhibit a higher prevalence of risk factors for cardiovascular diseases.

## METHODS

This cross-sectional study was conducted at a specialized gynecological endocrinology outpatient clinic located at a university hospital in northeastern Brazil. A convenience sample of 107 patients diagnosed with PCOS according to the Rotterdam criteria between April 2019 and June 2021 participated.[17] Ethical approval was granted under report number 3.127.233 (CAAE: 18082413920095292) and all participants provided informed consent.

PCOS diagnosis requires the presence of at least two of the following criteria: ovulatory dysfunction (e.g., oligomenorrhea or amenorrhea, usually defined as fewer than 8–9 menstrual periods per year), clinical or biochemical hyperandrogenism (such as hirsutism or elevated androgen levels), and polycystic ovarian morphology on ultrasound (≥20 follicles per ovary or ovarian volume >10 $cm^3$, or elevated antimüllerian hormone levels in adults). Other causes of hyperandrogenism or ovulatory dysfunction must be excluded.[17]

Participants completed a questionnaire that collected information on menstrual cycles, comorbidities, and personal and family medical histories. Exclusion criteria included prior diagnosis of androgen-secreting tumors, non-classic congenital adrenal hyperplasia, thyroid dysfunction, familial dyslipidemia, cardiovascular disease, arterial hypertension, diabetes mellitus type 1 or 2, and pregnancy. Additionally, patients with menarche occurring less than eight years prior to the study were excluded following the National Institutes of Health guidelines.[18]

Anthropometric assessments included weight, height, waist circumference, and hip circumference measurements. Body mass index (BMI) classified participants as normal weight (<25 $kg/m^2$), overweight (25–29.9 $kg/m^2$), or obese (≥30 $kg/m^2$), with obesity further categorized into grades I (30–34.9 $kg/m^2$), II (35–39.9 $kg/m^2$), and III (≥40 $kg/m^2$).[18]

Blood pressure was measured twice at a 10-minute interval, following the 7th Brazilian Guideline on Arterial Hypertension. Altered blood pressure was defined as systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg on the second measurement.[19] Although the Brazilian Guideline on Arterial Hypertension has since been updated, the use of the 7th edition remains appropriate for the data collection period and does not compromise the validity of the study findings.

Laboratory analyses included total cholesterol, high-density lipoprotein (HDL) cholesterol (HDL-c), LDL cholesterol (LDL-c), triglycerides, aspartate aminotransferase (AST), alanine aminotransferase (ALT), fasting glucose, and 2-hour post-glucose load levels via the oral glucose tolerance test (OGTT). Dyslipidemia was classified as isolated hypercholesterolemia (LDL-c ≥160 mg/dL), isolated hypertriglyceridemia (triglycerides ≥150 mg/dL), mixed hyperlipidemia (both elevated triglycerides and LDL-c), or low HDL-c (<50 mg/dL in women).[20]

Impaired glucose tolerance was diagnosed if the 2-hour OGTT glucose level was ≥140 mg/dL. Metabolic syndrome diagnosis requires the presence of at least three of the following: altered blood pressure (systolic ≥130 mmHg or diastolic ≥85 mmHg), low HDL-c (<50 mg/dL), elevated triglycerides (≥150 mg/dL), fasting glucose ≥100 mg/dL, and waist circumference ≥88 cm.[21,22]

Descriptive statistical analyses were performed using the absolute and relative frequencies. Pearson's chi-square test assessed associations between categorical variables and obesity (BMI ≥30). Poisson regression model with robust

variance estimated prevalence ratios (PR) and 95% confidence intervals (CI) for metabolic syndrome, dyslipidemia, impaired glucose tolerance, and altered blood pressure, using obesity as the independent variable. Statistical significance was set at $p < 0.05$. Analyses were performed using SPSS (Statistical Package for the Social Sciences, Chicago, USA).[23,24]

## RESULTS

This study included 107 women with a mean age of 27 ± 5 years, of whom 51 (47.7%) were classified as obese. Table 1 presents the sample characteristics.

Obese women with PCOS were significantly more likely to be diagnosed with metabolic syndrome, reduced HDL-c, impaired glucose tolerance, and altered systolic and diastolic blood pressure than non-obese women (Table 2).

Prevalence ratios (PR) for metabolic syndrome, dyslipidemia, impaired glucose tolerance, and altered blood pressure were significantly higher in obese women with PCOS, confirming that these comorbidities were more prevalent in patients with a BMI ≥30 at the time of diagnosis (Table 3).

**Table 1.** Sample characterization of women participating in the study (n = 107).

| Variables | n | % |
|---|---|---|
| Age, n (%) | 107 | 100 |
| Up to 25 years | 53 | 49,5 |
| > 25 years | 54 | 50,5 |
| Age at menarche, n (%) | | |
| Up to 12 years | 78 | 72,9 |
| ≥ 12 years | 29 | 27,1 |
| Place of residence, n (%) | | |
| Capital | 68 | 64,6 |
| Other city | 39 | 36,4 |
| BMI, n (%) | | |
| Normal | 22 | 20,6 |
| Overweight | 34 | 31,8 |
| Obesity grade I | 31 | 29,0 |
| Obesity grade II | 12 | 11,2 |
| Obesity grade III | 8 | 7,5 |

**Note:** Data are expressed as absolute (n) and relative (%) frequencies. Abbreviations: BMI, Body Mass Index; n, number.

**Table 2.** Association between obesity and metabolic syndrome, dyslipidemia, glucose metabolism abnormalities, and blood pressure alterations (n = 107).

| | | Obesity, n (%) | | |
|---|---|---|---|---|
| | n | Yes | No | p[a] |
| Total | 107 | 51 (47,7) | 56 (52,3) | |
| Metabolic syndrome, n (%) | | | | **<0,01** |
| Yes | 34 | 25 (73,5) | 9 (26,5) | |
| No | 62 | 19 (30,6) | 43 (69,4) | |
| HDL, n (%) | | | | **0,019** |
| HDL-c <50(dyslipidemia) | 80 | 43 (53,8) | 37 (46,2) | |
| Normal | 23 | 6 (26,1) | 17 (73,9) | |

**Note:** [a]Significance of the difference between groups was assessed using Pearson's chi-square test. Data are expressed as absolute (n) and relative (%) frequencies. Values in bold indicate significance at $P < 0.05$. Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; n, number.

Continue.

Conclusion.

**Table 2.** Association between obesity and metabolic syndrome, dyslipidemia, glucose metabolism abnormalities, and blood pressure alterations (n = 107).

| | | Obesity, n (%) | | |
|---|---|---|---|---|
| | **n** | **Yes** | **No** | **p[a]** |
| LDL, n (%) | | | | 0,882 |
| LDL-c ≥ 160 (isolated hypertriglyceridemia) | 11 | 5 (45,5) | 6 (54,5) | |
| Normal | 92 | 44 (47,8) | 48 (52,2) | |
| TGL, n (%) | | | | 0,236 |
| TGL ≥ 150 (isolated hypertriglyceridemia) | 30 | 17 (56,7) | 13 (43,3) | |
| Normal | 73 | 32 (43,8) | 41 (56,2) | |
| Mixed hyperlipidemia, n (%) | | | | 0,122 |
| Yes | 17 | 11 (64,7) | 6 (35,3) | |
| No | 86 | 38 (44,2) | 48 (55,8) | |
| Glucose intolerance, n (%) | | | | **0,002** |
| Yes | 26 | 19 (73,1) | 7 (26,9) | |
| No | 78 | 30 (38,5) | 48 (61,5) | |
| Systolic blood pressure, n (%) | | | | **<0,01** |
| Altered | 32 | 24 (75,0) | 8 (25,0) | |
| Normal | 75 | 27 (36,0) | 48 (64,0) | |
| Diastolic blood pressure, n (%) | | | | **<0,01** |
| Altered | 22 | 19 (86,4) | 3 (13,6) | |
| Normal | 85 | 32 (37,6) | 53 (62,4) | |

**Note:** [a]Significance of the difference between groups was assessed using Pearson's chi-square test. Data are expressed as absolute (n) and relative (%) frequencies. Values in bold indicate significance at P < 0.05. Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; n, number.

**Table 3.** Prevalence ratios of metabolic syndrome, dyslipidemia, glucose metabolism abnormalities, and blood pressure alterations in obese women with PCOS.

| | PR[a] (CI95%) | p |
|---|---|---|
| Metabolic syndrome | 3,28 (1,72 – 6,27) | **< 0,05** |
| Dyslipidemia | 1,28 (1,04 – 1,58) | **0,020** |
| Glucose intolerance | 3,05 (1,40 – 6,62) | **0,005** |
| Altered systolic pressure | 3,29 (1,63 – 6,66) | **0,001** |
| Altered diastolic pressure | 6,95 (2,19 – 22,12) | **0,001** |

**Note:** Values in bold are significant at the 5% level. [a]Obtained using the Poisson regression model with robust variance (independent variable: obesity). Abbreviations: PCOS-Polycystic ovary syndrome; PR, prevalence ratio; CI, confidence interval.

## DISCUSSION

In this study, the frequency of obesity was high, approaching 50% of the population studied. Prevalence ratios for metabolic syndrome, reduced HDL cholesterol, impaired glucose tolerance, and altered blood pressure were significantly higher in obese women diagnosed with PCOS. These findings highlight that in the northeastern Brazilian population of women with PCOS included in this study, the prevalence of obesity was elevated, and these comorbidities were more frequent in women with any degree of obesity.

The high prevalence of obesity may be explained by unhealthy dietary habits and sedentary lifestyles, which have commonly been reported in global studies.[7] A systematic

review also reported a high prevalence of obesity (50–80%) in women with PCOS.[8] One possible explanation is the presence of the human FTO gene on chromosome 16, which is associated with elevated BMI and is implicated in the pathophysiology of PCOS.[8] Conversely, the proposed association between PCOS and elevated obesity risk is not supported by findings from a Brazilian cohort study that demonstrated no significant difference in mean BMI between women with and without PCOS.[25] Additionally, a study comparing women with and without PCOS found that fibrin lysability was correlated with central obesity in patients with PCOS, suggesting an increased risk of cardiovascular disease in this population.[9]

Obesity and PCOS share many metabolic disturbances including hyperandrogenism and hyperinsulinemia, which form a feedback loop. Hyperandrogenism increases lipogenic gene expression and promotes fat accumulation, whereas hyperinsulinemia reduces hepatic SHBG production, increases free androgen availability, and favors obesity.[26] Conversely, obesity exacerbates insulin resistance, stimulating ovarian and adrenal androgen production and further fat accumulation.[8] Consequently, obese women with PCOS are more likely to develop metabolic syndrome, which is strongly associated with fat accumulation.[26]

Some Brazilian studies have also reported a higher prevalence of metabolic syndrome in obese women with PCOS.[10] However, contradictory to our results, a cross-sectional study of 322 women with PCOS in southeastern Brazil concluded that women with PCOS have a higher frequency of metabolic syndrome and its defining criteria regardless of BMI.[27]

In addition to metabolic syndrome, PCOS is associated with other comorbidities such as insulin resistance, which increases the risk of impaired glucose tolerance. A systematic review revealed lower insulin sensitivity in women with PCOS, with a higher BMI correlating with greater insulin resistance, which explains the higher prevalence of impaired glucose tolerance observed in obese women in this study.[28] Supporting our findings, a study of Brazilian women with PCOS found a higher prevalence of impaired glucose tolerance in obese versus non-obese patients.[15] Conversely, another study found no difference in the prevalence of impaired glucose tolerance between groups.[29]

Obesity and hyperglycemia driven by insulin resistance contribute to inflammation through tumor necrosis factor-alpha (TNFα) production, potentially increasing the risk of cardiovascular disease in women with PCOS.[13] Insulin resistance in PCOS may also increase the risk of hypertension via inflammatory signaling pathways, such as IKK-beta and JNK, leading to vasoconstriction and renal water retention.[14] Additionally, PCOS is associated with increased central adiposity and hemostatic alterations, creating a prothrombotic state that increases the cardiovascular risk.[13,14] While a study of Brazilian women with and without PCOS found no significant differences in blood pressure levels, our results support the association between obesity in PCOS and elevated blood pressure.[29]

Increased visceral fat accumulation in women with PCOS may predispose them to dyslipidemia.[12] Although no differences in HDL cholesterol levels were found in a national study comparing women with and without PCOS, our study found a significantly higher prevalence of dyslipidemia (HDL <50 mg/dL) in women with any degree of obesity.[15] Similarly, a Brazilian study of 44 adolescents with PCOS reported a higher prevalence of reduced high-density lipoprotein (HDL) in obese patients.[30] Another study of 102 women with PCOS from the same region as our participants found a high prevalence of HDL <50 mg/dL.[29]

These findings underscore the need for regular screening for metabolic syndrome, reduced HDL levels, and impaired glucose tolerance in women with PCOS. International guidelines recommend regular evaluations of weight, blood pressure, waist circumference, and lipid profiles, along with lifestyle modifications to prevent cardiovascular disease and diabetes.[1,17] These recommendations are particularly relevant to women with any degree of obesity.

However, this study has limitations, including the small convenience sample recruited from a single specialized outpatient clinic in north-eastern Brazil. The dietary and lifestyle habits of participants may have influenced the high prevalence of obesity, metabolic syndrome, impaired glucose tolerance, dyslipidemia, and altered blood pressure. These factors hinder the extrapolation of the results to populations in other regions or countries. Additionally, the cross-sectional design limits causal inferences between PCOS and an increased comorbidity prevalence.

## CONCLUSION

Young obese women with PCOS exhibit a higher prevalence of metabolic syndrome, impaired glucose tolerance, dyslipidemia, and altered systolic and diastolic blood pressures than non-obese women, indicating a higher risk of metabolic comorbidities related to obesity in this population. However, the prevalence of these comorbidities was also elevated in non-obese patients, suggesting that PCOS itself promotes metabolic comorbidities, regardless of BMI. Prospective studies are needed to evaluate whether women with PCOS have a higher lifetime risk of cardiovascular disease, with the aim of establishing appropriate primary and secondary prevention strategies.

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