Metabolic profile of the different phenotypes of polycystic ovary syndrome in two Latin American populations

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Objective: To evaluate the metabolic profile of Chilean and Argentinian women with polycystic ovary syndrome (PCOS) according to the Rotterdam criteria.
Design: Observational cross-sectional study.
Setting: Academic centers.
Patient(s): Women with PCOS, aged 18–39 years: 220 Chilean ($PCOS_{Ch}$) and 206 Argentinian ($PCOS_{Ar}$).
Intervention(s): Physical examination, fasting blood samples for androgens, gonadotropins, metabolic parameters, and a transvaginal ultrasound.
Main Outcome Measure(s): Comparative analysis of the metabolic profile in both populations divided into four phenotypes.
Result(s): The distribution of the different phenotypes was different in both populations. $PCOS_{Ch}$ women showed a higher body mass index and a higher percentage of metabolic syndrome in all phenotypes compared with the $PCOS_{Ar}$ women. The $PCOS_{Ar}$ women exhibited a statistically significantly higher diastolic blood pressure in phenotypes A, B, and C and a higher percentage of hypertension in phenotypes A and D compared with the $PCOS_{Ch}$ women.
Conclusion(s): The data show differences in the metabolic profile of both populations. $PCOS_{Ch}$ women presented with greater metabolic alterations such as dysglycemia and dyslipidemia and a higher prevalence of metabolic syndrome, independent of the phenotype. The $PCOS_{Ar}$ patients showed more elevated blood pressure. Ethnic diversity associated with environmental factors are fundamental elements in the analysis of the PCOS phenotypes. (Fertil Steril® 2014;■:■–■. ©2014 by American Society for Reproductive Medicine.)
Key Words: Argentina, Chile, metabolic syndrome, polycystic ovary syndrome, Rotterdam phenotypes

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Polycystic ovary syndrome (PCOS) is a hyperandrogenic disorder associated with chronic oligo-ovulation and polycystic ovary morphology. It is the most common cause of hyperandrogenism, with a prevalence reaching up to 15% when using the Rotterdam criteria described in 2003 (1). Hyperandrogenism and chronic anovulation are the main elements of this definition; the ultrasound pattern of polycystic ovaries is the third

element incorporated in the 2003 consensus (1). According to this definition, the diagnosis of PCOS may be established with two of the three criteria described, generating four different phenotypes:

Phenotype A: hyperandrogenic women with oligoanovulation and transvaginal ultrasound with polycystic ovarian morphology (H/O/PCOM).

Phenotype B: women with hyperandrogenism, oligoanovulation, and without PCOM (H/O).

Phenotype C: hyperandrogenic women with ovulatory cycles and PCOM (H/PCOM).

Phenotype D: normoandrogenic women with oligoanovulation and PCOM (O/PCOM).

Recently, it has been observed that each PCOS phenotype is associated with a different metabolic risk. Most studies have shown that hyperandrogenism is the main factor for the development of metabolic and cardiovascular alterations, with phenotypes A and B having a higher metabolic risk than phenotype D, whose risk is comparable to that of control women (2, 3). However, these phenotypes may vary in individuals and may be modified by changes in weight, treatment, and/or healthy lifestyle factors (4).

It has been proposed that the development of PCOS and its phenotypic expressions may be influenced by genetic and environmental factors that can affect a woman from her intrauterine life until the reproductive stage (4, 5). In this regard, racial and ethnic characteristics are a very important genetic aspect to be considered in PCOS and its phenotypic expressions (6). This background may influence the clinical manifestations of PCOS. For instance, Middle Eastern women have a greater prevalence of hirsutism (2) whereas among East Asian women hirsutism is less common (7, 8). In Indian women, acne has been described as the most prevalent clinical expression of hyperandrogenism (9).

The presence of the metabolic syndrome has been associated with PCOS with variable frequency; its prevalence is lower in East Asian women (7, 8) and higher in women of African, South Asian, and Hispanic descent (2, 10). A northern California study of women with PCOS found that, compared with white patients, black and Hispanic patients were more likely and Asian patients less likely to be obese, the Asian and Hispanic women were more likely to have diabetes, and the black women were more likely and Hispanic women less likely to have hypertension (10).

The phenotypic distribution of PCOS in Latin American populations is only partially known. Thus, our study compares the metabolic profile of women with PCOS from two neighboring countries with different ethnic compositions. Argentina, and especially the city of Córdoba, has been influenced by a large, mainly European immigration wave composed primarily of Italians and secondarily of Spaniards (11). In contrast, in Chile over 65% of the population is of Spanish descent, with the phenotypic characteristics of a mostly white population: the average proportion is 60% Hispanic and 40% Amerindian (12, 13). Our study compares the metabolic profile, classified into the four phenotypes described according to the Rotterdam criteria, of 220 women with PCOS from Santiago de Chile ($PCOS_{Ch}$) and 206 women with PCOS from the province of Córdoba, Argentina ($PCOS_{Ar}$), who have a different ethnic background.

MATERIALS AND METHODS

Patients

We studied 220 $PCOS_{Ch}$ women who were treated at the polyclinic of the Department of Endocrinology and Metabolism of Universidad de Chile in Santiago (Chile) and 206 $PCOS_{Ar}$ women who were treated at the Department of Endocrinology and Diabetes of Universidad de Córdoba (Argentina), both academic health centers serving patients from a socioeconomically middle-class area. All the women were between 18 and 39 years old and had a body mass index (BMI) between 18 and 35. The study was approved by the institutional review boards of both academic centers, and all participants gave their written informed consent.

An analysis of the ethnic background in both countries was conducted. All women belonged to the white race. The $PCOS_{Ch}$ group was composed of women who were 90% Hispanic-Amerindian mixture, 7% Amerindian, and 3% other races. The $PCOS_{Ar}$ group was composed of 87% of European, predominantly Italian, descent; 10% Hispanic-Amerindian mixture; and 3% other ethnicities. The differences in the distribution pattern of ethnicities between the two groups was statistically significant ($P<.001$). Comparisons were made only between the Chilean and Argentinean country groups. We did not make comparisons between the various ethnic groups because it would have meant combining only 10% of the Argentinean group with 90% of the Chilean group; this would have left other two groups too small for analysis and ignored the potential lifestyle differences between the country groups.

The diagnosis of PCOS was established according to the Rotterdam criteria (1), including at least two of the following elements:

Hyperandrogenism (H): modified Ferriman-Gallwey score ≥ 8 and/or total serum testosterone (T) ≥ 80 ng/dL (≥ 2.77 nmol/L).

Ovulatory dysfunction (O): oligomenorrhea (cycles >35 days) or amenorrhea (no menses in the last 6 months), negative pregnancy test, and progesterone level <4 ng/mL (12.72 nmol/L) before beginning of the study.

Polycystic ovaries at transvaginal ultrasound (PCOM): ≥ 12 follicles measuring 2–9 mm in diameter and/or increased ovarian volume (>10 mL) in at least one ovary.

The exclusion criteria were other causes of hyperandrogenism (Cushing syndrome, congenital adrenal hyperplasia, or androgen-secreting tumors), a previous diagnosis of type 2 diabetes mellitus and/or treatment with insulin-sensitizing drugs, or use of contraceptives, antiandrogens, or glucocorticoids 6 months before the beginning of the study. Moreover, all participants had normal thyroid function, normal prolactin levels, and a follicle-stimulating hormone (FSH) level in the