

## ENDOCRINOLOGY

# Association Between the Polycystic Ovary Syndrome and the Metabolic Syndrome in Puerto Rico

MARIELSA RABELO ACEVEDO, MD; MARGARITA RAMÍREZ VICK, MD

Polycystic ovary syndrome (PCOS) affects mostly young women causing chronic anovulation, hyperandrogenism, hirsutism and obesity with android pattern. The prevalence of the metabolic syndrome (abnormal glucose metabolism, dyslipidemia, hypertension and increased waist circumference) in PCOS is not defined although both have a common etiologic factor: insulin resistance. This retrospective study from medical records examined the presence of obesity and features of the metabolic syndrome in women with PCOS. The metabolic syndrome was defined as presence of two or more of the following signs: abnormal glucose metabolism, hypertriglyceridemia, low HDL, and hypertension. Thirty nine records of patients with PCOS were reviewed. The mean age was 29.4 years and the body mass index was 36 kg/

m<sup>2</sup>. Hypertriglyceridemia was present in 43%, low HDL in 71%, hypertension in 36%, impaired glucose tolerance in 10% and diabetes mellitus type 2 in 37%. The metabolic syndrome was identified in 44% of sampled women with PCOS. These findings indicate that women with PCOS are at increased risk of diabetes mellitus type 2 at a young age. PCOS patients have higher prevalence of the metabolic syndrome than the rest of the population and thus are at increased risk of cardiovascular disease even if they don't develop diabetes mellitus type 2.

*Key words: Polycystic ovary syndrome, Metabolic syndrome, Insulin resistance, Anovulation, Cardiovascular risk, Hyperandrogenism, Impaired glucose tolerance*

Stein and Leventhal first used the term polycystic ovary syndrome (PCOS) in 1935, referring to a condition suffered by women with menstrual dysfunction, infertility, androgen excess, hirsutism and obesity (1). It was not until 1980 that metabolic disturbances were recognized as part of this syndrome. Polycystic ovary syndrome is the most common endocrinopathy in young women nowadays. PCOS affects 5-10% of women of reproductive age (2). It's the most frequent cause of infertility due to anovulation in the United States (US).

The clinical features of PCOS include chronic anovulation with irregular and unpredictable uterine bleeding; hyperandrogenism with growth of terminal hair in the face, chest and periumbilical area; obesity with an android pattern (increased waist to hip ratio); and polycystic ovaries present in about 80% of women. Polycystic ovaries morphology is not essential for the diagnosis, thus the name of the syndrome may be misleading. Insulin resistance is cornerstone in women with PCOS.

The metabolic syndrome describes a condition characterized by decreased sensitivity of tissues to the actions of insulin, which in turn induces an increased insulin secretion (3). This metabolic dysfunction leads to a cluster of systemic anomalies with serious clinical consequences. The components of the metabolic syndrome include: impaired glucose tolerance or impaired fasting glucose, abnormal uric acid metabolism, dyslipidemia (high triglycerides, low HDL, small, dense LDL), hypertension, prothrombotic factors, elevated markers of inflammation and endothelial dysfunction. The prevalence of metabolic syndrome is worrisome: one in 3-4 American adults have metabolic syndrome while 36% of Latino/ Hispanics have metabolic syndrome.

Some patients with metabolic syndrome eventually become diabetic (diabetes mellitus type 2), and, even though, the majority of these subjects with metabolic syndrome do not become diabetic, they do have a significantly elevated risk of cardiovascular disease.

The metabolic syndrome is associated with cardiovascular disease (4), and women with polycystic ovary syndrome are known to have insulin resistance and are at risk for the metabolic syndrome, but the prevalence of the metabolic syndrome in women with PCOS is not documented (5).

Address correspondence to: Dr. Margarita Ramírez Vick, Endocrinology Section, Department of Medicine, Medical Sciences Campus, University of Puerto Rico, PO Box 365067, San Juan, PR 00936-5067.

The purpose of this study is to define the prevalence of obesity and features of the metabolic syndrome (hypertension, hypertriglyceridemia, abnormal glucose metabolism, low HDL) in Puerto Rican women with polycystic ovary syndrome.

### Methods

This study was conducted through review of records of the Endocrinology section at the University Hospital of Puerto Rico. From the records of patients with PCOS, the following data was gathered: age, weight and height, triglyceride levels, HDL levels, fasting blood sugar and results of 2 hour 75 gram oral glucose tolerance test. Each patient's body mass index (BMI) was calculated in kg/m<sup>2</sup>. Mean for age and BMI were calculated as well as standard deviation. The percentage of women with PCOS and hypertriglyceridemia, low HDL, impaired fasting or impaired glucose tolerance and hypertension were calculated.

Although there are no recommendations for a minimum number of criteria to be present in order to diagnose the metabolic syndrome, the American College of Endocrinology (ACE) has defined, for epidemiological purposes, the metabolic syndrome as the presence of 2 or more of the following in an individual at risk: 1) abnormal plasma glucose: fasting plasma glucose 110-125 mg/dL or 120 min post 75 gm glucose challenge 140-200 mg/dL; 2) triglycerides > 150 mg/dL; 3) HDL cholesterol <50 mg/dL; 4) blood pressure >130/85 mm Hg. For each woman with PCOS, the above criteria were used to define the presence of the metabolic syndrome using the data available on their medical records. The percentage of women with PCOS fulfilling the criteria for the metabolic syndrome was calculated.

### Results

Thirty nine records of women with polycystic ovary syndrome were identified. The mean age was 29.4 year old with a standard deviation of 8.6 (age range from 19 y/o to 57 y/o). Their mean BMI was 36 kg/m<sup>2</sup> with a range of 20 to 56 kg/m<sup>2</sup>. (See Table 1) A BMI higher than 25 kg/m<sup>2</sup> was present in 89.5% of women with PCOS (34/38), and BMI greater than 30 kg/m<sup>2</sup> was present on 87% of women with PCOS (33/38). Forty three percent of women with PCOS (9/21) have triglyceride levels greater than 150 mg/dL and seventy one percent of women with PCOS (12/17) have HDL levels less than 50 mg/dL. In our study thirty six percent of women with PCOS (14/39) had blood pressure greater than 130/85 mm Hg. Impaired glucose tolerance was identified in 10% of women with PCOS (3/30) and diabetes mellitus type 2 was present in 37% of women

**Table 1.** Presence of Components of the Metabolic Syndrome in Puerto Rican Women PCOS in Puerto Rico

Metabolic syndrome component	Prevalence in women with PCOS
BMI>25	89.5%
Triglycerides > 150 mg/dL	43%
HDL < 50 mg/dL	71%
Hypertension	36%
Impaired glucose tolerance	10%
Diabetes mellitus 2	37%
Abnormal glucose metabolism	47%
Metabolic syndrome	44%

with PCOS (11/30) and an abnormal glucose metabolism was present in 47% of women with PCOS (14/30).

Using the criteria defined by the ACE, the metabolic syndrome was identified in 44% (17/39) of sampled women with PCOS.

### Discussion

In Puerto Rican women with PCOS, obesity is almost universal. This situation will cause these women to have two types of insulin resistance: one caused intrinsically by PCOS and a second one due to obesity (6). The great majority of these patients with PCOS are at risk of the deleterious consequences of obesity.

Women with PCOS have higher fasting insulin levels than their counterparts without the syndrome and when exposed to a hyperglycemic stimulus, they have an exaggerated increase in insulin levels (7). Insulin resistance produces hyperinsulinemia to keep euglycemia. This compensatory hyperinsulinemia stimulates the ovaries to produce testosterone, decreases the levels of sex hormone binding globulin and alters the release of pituitary gonadotropins producing an anovulatory state (8). It is estimated that 30-35% of women with PCOS have impaired glucose tolerance, while 2-10% of women with PCOS have diabetes mellitus type 2. These numbers are aggravated in the presence of obesity: 30-50% of obese women with PCOS have impaired glucose tolerance or diabetes mellitus type 2 by age 30 (9). In Puerto Rico, the prevalence of diabetes mellitus, specially type 2, is particularly high (10). Hispanic women of Caribbean origin with polycystic ovary syndrome have been reported to have greater insulin resistance than comparable non Hispanic white women (11). In Puerto Rico in a study published in 2000, it was found that 4.8% of women with PCOS have impaired fasting glucose while 2.4% have diabetes mellitus type 2 (12).

This would suppose that a considerable number of these patients have problems with glucose metabolism and this is consistent with the finding that almost half of sampled

patients with PCOS (47%) have abnormal glucose metabolism (10% have impaired glucose tolerance and 37% have diabetes mellitus type 2). This is of particular importance, since PCOS has a high prevalence in the US especially in the Latin population, and many women would be at high risk of diabetes mellitus type 2 at a young age.

The difference in prevalence of abnormal glucose metabolism found in our study from that reported in the literature (12) could be attributed to the fact that the oral glucose tolerance test was not used in previous studies, which is a more sensitive tool for identifying impaired glucose tolerance and diabetes mellitus type 2 compared to fasting blood glucose.

More than two thirds of PCOS patients have low HDL, more than one third have hypertriglyceridemia, and the same percentage was found with hypertension. All these are known to be cardiovascular disease risk factors and were identified in a considerable number of this group of young women.

The components of the metabolic syndrome include: impaired glucose tolerance or impaired fasting glucose, abnormal uric acid metabolism, dyslipidemia (high triglycerides, low HDL, small, dense LDL), hemodynamic changes (sympathetic nervous system activity, renal sodium retention, hypertension), BMI >25 kg/m<sup>2</sup> (or waist circumference >40 inches in men, >35 inches in women), age >40 years, prothrombotic factors, elevated markers of inflammation (C-reactive protein, WBC) (13), and endothelial dysfunction (mononuclear cell adhesion, plasma concentration of cellular adhesion molecules, plasma concentration of asymmetric dimethylarginine and endothelial dependent vasodilatation). Insulin causes the production of nitric oxide which leads to vasodilatation and hemodynamic changes. Insulin also leads to the production of cellular adhesion molecules to which monocytes adhere forming atheromatous plaques that when ruptured lead to vessel occlusion. Presence of the metabolic syndrome confers an increased risk of coronary heart disease and cardiovascular disease mortality.

The metabolic syndrome was identified in 44% of sampled women with PCOS. This is a considerably higher prevalence when compared to that found in the general population (30% in Americans, 36% in Hispanics).

It is important that every patient with PCOS be evaluated for the metabolic syndrome. Identifying the metabolic syndrome and recognizing the risk of metabolic syndrome in PCOS is of clinical benefit, because it emphasizes the fact that these young women are at risk of cardiovascular disease even if they don't develop diabetes mellitus type 2. It is also necessary to acknowledge that women with PCOS are one of the groups at highest risk of diabetes mellitus type 2 so this should be part of their evaluation and follow-

up.

The pathogenesis of PCOS and the role insulin resistance has in this condition should guide treatment of PCOS. At present, oral contraceptive pills are part of their treatment, but if it is proven that women with PCOS are likely to have the metabolic syndrome and to be at high risk for cardiovascular disease, oral contraceptive pills may be considered deleterious instead of helpful due to their estrogen content and prothrombotic potential (14).

To decrease insulin resistance and prevent the evolution to diabetes mellitus type 2, lifestyle changes, such as weight loss, exercise and diet have proven effective and should be an important part of management in patients with PCOS, although it is well known that to keep lifestyle changes at long term is difficult for most patients. Insulin sensitizers (metformin and thiazolidinediones) have also demonstrated effectiveness in treatment of PCOS (15, 16, 17, 18).

It must be emphasized that women with polycystic ovary syndrome come to our clinics complaining of hirsutism and irregular menstrual bleeding, but they need and deserve a complete evaluation of their risk factors for the metabolic syndrome and treatment directed to the cause of their problem.

The limitations of our study are that it consisted of a small sample of 39 medical records and some of the data needed for our study were missing. Long term studies in patients with PCOS are needed to determine their cardiac morbidity and mortality and to guide us in their treatment.

## Resumen

El síndrome de ovarios poliquísticos afecta a mujeres jóvenes, causando anovulación crónica, hiperandrogenismo, hirsutismo y obesidad con un patrón androide. La prevalencia del síndrome metabólico (metabolismo anormal de glucosa, dislipidemia, hipertensión y aumento en la cintura) en el síndrome de ovarios poliquísticos no está definida aunque comparten una etiología en común: resistencia a la insulina. Este estudio retrospectivo de expedientes médicos examinó la presencia de obesidad y características del síndrome metabólico en mujeres con el síndrome de ovarios poliquísticos. El síndrome metabólico se definió como la presencia de dos o más de los siguientes hallazgos: anomalías en el metabolismo de la glucosa, hipertrigliceridemia, HDL bajo e hipertensión arterial. Se identificaron 39 expedientes de pacientes con el síndrome de ovarios poliquísticos, con una edad media de 29.4 años e índice de masa corporal de 36 kg/m<sup>2</sup>. La hipertrigliceridemia estaba presente en 43%, el HDL bajo en 71%, la hipertensión en 36%, la intolerancia a la glucosa en 10% y diabetes mellitus tipo 2 en 37%. El síndrome

metabólico se identificó en 44% de las mujeres muestreadas con el síndrome de ovarios poliquísticos. Estos hallazgos indican que las mujeres con el síndrome de ovarios poliquísticos están a mayor riesgo de diabetes tipo 2 a menor edad y tienen una mayor prevalencia del síndrome metabólico que el resto de la población.

Las pacientes del síndrome de ovarios poliquísticos están a riesgo de enfermedad cardiovascular aún si no desarrollan diabetes.

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