Subclinical hypothyroidism in young women with polycystic ovary syndrome: an analysis of clinical, hormonal, and metabolic parameters

Cristina Laguna Benetti-Pinto, M.D., Ph.D.,[a] Vanessa Ribeiro Santana Berini Piccolo, M.D.,[a] Heraldo Mendes Garmes, M.D., Ph.D.,[b] and Cássia Raquel Teatin Juliato, M.D., Ph.D.[a]

[a] Department of Obstetrics and Gynecology and [b] Endocrinology Unit, Department of Clinical Medicine, School of Medical Sciences, State University of Campinas, Campinas, Brazil

Objective: To analyze the relationship between selected clinical and metabolic parameters in young women with polycystic ovary syndrome (PCOS) and normal thyroid function or subclinical hypothyroidism (SCH).
Design: A cross-sectional cohort study.
Setting: Tertiary care clinic.
Patient(s): Women diagnosed with PCOS according to the Rotterdam criteria (n = 168).
Intervention(s): Clinical, hormonal, and metabolic parameters were evaluated. SCH was defined as TSH levels of 4.5–10 mIU/L.
Main Outcome Measure(s): Separately, PCOS and SCH exert adverse effects on metabolic parameters; however, in conjunction their effect is unclear. This study evaluated whether SCH in women with PCOS affects clinical, hormonal, and metabolic parameters.
Result(s): The mean age of the 168 women was 24 ± 5.8 years. Mean body mass index was 33.4 ± 8.2 kg/m^2. Thyroid function was normal in 149 women, and 19 had SCH. Only serum low-density lipoprotein cholesterol and PRL levels were significantly higher in the women with SCH (122.6 ± 25.6 mg/dL and 17.7 ± 7.7 ng/mL, respectively) compared with those with normal thyroid function (105.6 ± 33 mg/dL and 14 ± 10.3 ng/mL, respectively).
Conclusion(s): In young women with PCOS, SCH is associated with higher low-density lipoprotein cholesterol levels, albeit with no changes in other lipid profile parameters, insulin resistance, or phenotypic manifestations. This study adds to current evidence supporting an association between PCOS and SCH. (Fertil Steril® 2013;99:588–92. ©2013 by American Society for Reproductive Medicine.)
Key Words: Polycystic ovary syndrome, insulin resistance, subclinical hypothyroidism, serum lipids

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Polycystic ovary syndrome (PCOS) is a common endocrine metabolic disorder that affects 5%–10% of women of reproductive age (1, 2). Various factors involved in PCOS are also present in women with hypothyroidism. Some authors have affirmed that hypothyroidism is a state of insulin resistance (IR), and IR has also been considered to be the principal factor in the genesis of PCOS (3). In cases of PCOS alone and in cases of hypothyroidism alone, changes take place in lipid metabolism and there is a risk of arterial hypertension and endothelial dysfunction in addition to ovulatory dysfunction. Consequently, the association between thyroid dysfunction and the clinical and laboratory parameters of PCOS has become the object of recent studies; however, this relationship remains unclear, particularly when the two conditions occur in conjunction (4–9).

More recently, the metabolic alterations present in subclinical hypothyroidism (SCH) have been investigated, as well as their association with IR. Some studies conducted in the general population have shown changes in lipid metabolism with an increase in total cholesterol (CHOL) and in high-density lipoprotein cholesterol (HDL-C) (6, 10)

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Reprint requests: Cristina Laguna Benetti-Pinto, M.D., Ph.D., Department of Obstetrics and Gynecology, School of Medical Sciences, State University of Campinas (UNICAMP), Alexander Fleming, 101, Cidade Universitária, 13083-881 Campinas, SP, Brazil (E-mail: laguna.unicamp@gmail.com).

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as well as a greater risk of cardiovascular disease in SCH associated with IR (11). However, others have reported no negative effect on these parameters (12, 13), reinforcing the need for further studies, particularly in better-defined populations, such as women with PCOS. A study conducted in 2011 in women with PCOS and normal thyroid function or SCH revealed higher triglyceride (TRIG) levels in SCH; however, there were no differences in any of the other parameters related to lipid metabolism or in clinical parameters such as body mass index (BMI) (6).

Considering the association between PCOS, IR, and the metabolic syndrome, as well as the effect of the thyroid on these same factors and the sparse evidence of an interaction between SCH and PCOS, the present study was developed to analyze the relationship between SCH and clinical and metabolic parameters in young women with PCOS.

SUBJECTS AND METHODS

Subjects

A cross-sectional cohort study was conducted in which 168 women with a diagnosis of PCOS defined in accordance with the Rotterdam criteria (14) were evaluated. The women were all receiving care as outpatients at the Department of Gynecology and Obstetrics, School of Medical Sciences, State University of Campinas. The women were included at the time of diagnosis and had not yet initiated treatment with hormones or hypoglycemic drugs.

Women with chronic diseases such as overt hypothyroidism and hyperthyroidism, kidney or liver failure, hyperprolactinemia, late-onset adrenal hyperplasia, and diabetes were excluded from the study. The study was approved by the institution's Internal Review Board (IRB no. 376/2010).

Methods

Anthropometric data (weight, height, waist and hip circumferences) were recorded, arterial blood pressure was measured, and a clinical evaluation was performed to verify the presence of androgenic manifestations in all of the women included in the study. BMI was calculated from the ratio between the woman's weight and the square of her height, expressed as kg/m^2. Hirsutism was classified in accordance with the Ferriman-Gallwey index over nine body areas (15).

Thyroid-stimulating hormone (TSH), free thyroxine (FT_4), free testosterone (T), total T, DHEAS, PRL, fasting glucose, fasting insulin, TRIG, CHOL, HDL-C, and low-density lipoprotein cholesterol (LDL-C) levels were measured. The blood samples were obtained from peripheral veins during the 3rd to 9th days of the menstrual cycle or 60 days after the last menstrual period after a fasting period of ≥ 12 hours.

Glucose levels were measured with the use of an enzymatic colorimetric method (Roche/Hitachi 904/911 Modular ACN 249). Insulin was measured with the use of a chemiluminescent immunometric method (Immulite/Immulite 1000; Siemens). CHOL, HDL-C, LDL-C, and TRIG were analyzed with the use of an enzymatic colorimetric test (Roche/Hitachi Modular ACN). DHEAS was measured with the use of a chemiluminescent immunometric method (Immulite/Immulite 1000 DHEA-S04). TSH, FT_4, PRL and total T levels were measured by electrochemiluminescence (Cobas e411). Free T was measured by radioimmunoassay (Beckman Coulter DSL 4900).

IR was also evaluated with the use of the homeostatic model assessment of insulin resistance (HOMA-IR), which represents an indirect evaluation of IR made by measuring endogenous insulin and glucose after a 12-hour fasting period. HOMA-IR values >2.7, the cutoff point established for a diagnosis of IR in the Brazilian population, were taken into consideration in the present study (16, 17).

Subclinical hypothyroidism was defined as serum TSH levels of 4.5–10 mIU/L (18), and all of the subjects included in the study had normal FT_4 levels.

Statistical Analysis

The results are described as mean ± SD. Significance level was defined at 5%, and the software used for the analysis was the SAS statistical software package, version 9.1.

The independent variables were evaluated in accordance with the classification of TSH <4.5 mIU/L (normal thyroid function) or TSH 4.5–10 mIU/L (SCH) with the use of the Student *t* test and the Mann-Whitney test. The correlation between TSH values and the independent variables was evaluated with the use of Spearman rank correlation coefficient.

RESULTS

The 168 women with PCOS were young (mean age 24.19 ± 5.78 years), obese (BMI 33.45 ± 8.23 kg/m^2), and hirsute (Ferriman-Gallwey index 12.05 ± 4.37). Mean fasting glucose, fasting insulin, HOMA-IR, and TSH were 87.55 ± 14.07 mg/dL, 16.31 ± 10.8 μIU/mL, 3.63 ± 2.75, and 2.71 ± 1.57 mIU/L, respectively.

A diagnosis of SCH was established in 11.3% of the women with PCOS (n = 19), with a mean TSH level of 6.1 ± 1.2 mIU/L. The remaining 149 women had normal thyroid function (TSH 2.3 ± 1.0 mIU/L). There was no difference between the two groups regarding age, BMI, hirsutism as evaluated by the Ferriman-Gallwey index, systolic blood pressure, diastolic blood pressure, waist circumference, or hip circumference (Table 1).

In the evaluation of lipid metabolism, a statistically significant difference was found in LDL-C levels, which were higher in the women with SCH compared with those with normal thyroid function (122.58 ± 25.61 mg/dL vs. 105.64 ± 32.97 mg/dL, respectively; $P=.04$). PRL levels also were higher in the group of women with SCH (Table 1). There was no difference between the women with PCOS and normal thyroid function and those with PCOS and SCH regarding any of the other metabolic parameters or the hormonal parameters evaluated.

A weak positive correlation was found between TSH and LDL-C: The higher the TSH level, the higher the serum LDL-C level ($R = 0.19$; $P=.04$).

DISCUSSION

The present results show that 11.3% of the women with PCOS had SCH, with higher serum LDL-C levels than the women with normal thyroid function. A positive correlation was