Thyroid Function Status and Thyroid Hormones Disturbances in Polycystic Ovarian Syndrome

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Abstract- A close association between thyroid problems and polycystic ovarian syndrome (PCOS) has been recently raised suggesting common pathophysiological link between the two disease conditions. The present study aimed to assess the status of thyroid hormones in women with PCOS with the aim of clarifying the link between PCOS and thyroid abnormalities. This cross-sectional study was performed on 87 consecutive women aged 31 to 50 years finally diagnosed as PCOS based on the Rotterdam diagnostic criteria. Venous blood sample was extracted from all subjects to determine the levels of fasting blood glucose, hemoglobin A1C, serum insulin level and also thyroid hormones in a single laboratory. The mean serum level of TSH was 3.02±1.19 µIU/ml, the mean level of T4 was 7.22±1.81 µg/dl, and the mean level of T3 was 1.23±0.18 ng/ml. Based on the normal values of thyroid hormones, none of the PCOS patients had abnormal levels of TSH and T3 hormones. Also, normal level of T4 was revealed in 90.8% of patients, while only 6.9% and 2.3% had T4 level lower than and higher than the normal range respectively. Using the correlation tests, none of the thyroid hormones was linearly associated with age, weight, BMI, the value of FBS or the levels of lipid profiles. The high prevalence rate of overweight to obesity (97.7%), hypertriglyceridemia (65.5%), and uncontrolled glycemic status (21.8%) were prominent in PCOS women. In our observation, we found no significant link between abnormal changes in thyroid hormone and PCOS.

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Keywords: Thyroid gland; Thyroid hormones; Polycystic ovarian syndrome

Introduction

Polycystic ovarian syndrome (PCOS) has been identified as one of the most common endocrine disorders with an overall incidence ranged between 5% to 10% in reproductive ages (1,2). This phenomenon is characterized by a heterogenic feature including chronic anovulation related to excessive production of androgens such as testosterone and androstenedione along with some metabolic disturbances such as insulin resistance secondary to defects in insulin receptor signaling pathways, hyperinsulinemia, deregulation of glucose and lipid metabolism due to lowering the level of adiponectin secreted by adipocytes, and finally obesity (3-5). Due to the close association of PCOS with metabolic disturbances, the increased risk for cardiovascular and metabolic disorders is not unexpected (6). Furthermore, the likelihood of endometrial hyperplasia and cancer in such patients has been shown (7,8). In this regard, international societies such as the American College of Endocrinology and the American Association of Clinical Endocrinologists recommend the screening for metabolic and endocrine abnormalities in all women with the diagnosis of PCOS especially by age 30 years (9,10). In line with the increased risk for endocrine disorders in PCOS, some recent studies have also revealed the elevated risk for thyroid disorders in PCOS (11,12). Some investigations have pointed the increased risk for hypothyroidism and also autoimmune thyroiditis in the background of PCOS (13). More interestingly, some ovarian-related changes including the appearance of cystic lesions and increasing the size and volume of ovaries are commonly realized in both PCOS and thyroid disorders (14,15). Despite different pathophysiological natures in these two disorders, the presence of common predisposing factors and observing some aspects of

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autoimmunity in both disorders are suggestive of shared pathophysiological rings between the two disease conditions. Therefore, the present study aimed to assess the status of thyroid hormones in women with PCOS with the aim of clarifying the link between PCOS and thyroid abnormalities.

Materials and Methods

This cross-sectional study was performed on 87 consecutive patients aged 31 to 50 years who referred to Gynecology clinic at Imam Khomeini hospital in Tehran, Iran between 2014 and 2015 that were finally diagnosed as PCOS based on the presence of at least two of the Rotterdam diagnostic criteria for PCOS including oligo/anovulation, hyperandrogenism, hirsutism or less commonly male pattern alopecia, raised FAI or free testosterone, or polycystic ovaries on ultrasound (at least 12 cysts with the size of 2 to 9 mm). The exclusion criteria were the history of Cushing's disease, hyperprolactinemia, adrenal hyperplasia, history of any intervention on thyroid glands, or medication with thyroid hormones, or history of using estrogenic or androgenic drugs. After collecting baseline characteristics and medical history of the patients by interviewing in the clinic, 5ml of venous blood sample was extracted from all subjects to determine the levels of fasting blood glucose, hemoglobin A1C, serum insulin level, and thyroid hormones by ELISA technique in a single laboratory. All parameters were assessed according to manufacturer's instruction by commercial kits (AccuBindELISA Microwells, Monobind, Inc. Lake Forest, CA, USA). The study endpoint was to determine the level of thyroid hormones and compared it with the normal standard ranges summarized in table 1. The study protocol was approved by the ethics' committee at Tehran University of Medical Sciences. The written informed consent was obtained from all participants after explaining the details of interventions and the goals of the study.

Table 1. The standard references for the normal ranges of hormones

Hormone	Normal range	Sensitivity of kit
T3	0.52-1.85 ng/ml	0.04 ng/ml
T4	4.4-10.8 µg/dl (for men) 4.8-11.6 µg/dl (for women)	3.2 µg/dl
TSH	0.39-6.16 µIU/ml	0.078-0.027 µIU/ml
Free T3	1.4-4.2 pg/ml	
Free T4	0.8-2.0 ng/ml	

For statistical analysis, results were presented as the mean±standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnoff test. The linear association between the quantitative variables was examined using the Pearson's or Spearman's correlation test. For the statistical analysis, SPSS software, version 16.0 for Windows (SPSS Inc., Chicago, IL) was used. *P* of 0.05 or less were considered statistically significant.

Results

Study population

Totally 87 women with PCOS were assessed. The mean age of participants was 34.64±7.71 years ranged between 22 to 60 years, the mean weight was 89.21±11.09 kg ranged 63 to 128 kg, and the mean body mass index (BMI) of 31.21±3.95 kg/m^2 ranged 24.0 to 41.1 kg/m^2. Considering a BMI 25 to 29.9 as overweight and >29.9 kg/m^2 as obesity, 43.7% were overweight, and 54.0% were obese. The mean values and the ranges of laboratory parameters are presented as table 2. According to the definition of hyperglycemia as fasting blood sugar higher than 126 mg/dl, hypertriglyceridemia as serum triglyceride level higher than 150 mg/dl, and hypercholesterolemia as serum total cholesterol level higher than 240 mg/dl, 13.8% were hyperglycemic, 65.5% had hypertriglyceridemia, and only 4.6% had hypercholesterolemia. Also, 17.2% had serum HDL lower than 40 mg/dl, and none of the subjects had serum LDL higher than 160 mg/dl. Considerably, 21.8% had uncontrolled glycemic status with serum hemoglobin A1C higher than 5.7%. The serum creatinine level was in the normal range (<1.5 mg/dl) in all women.

Table 2. The mean and range of the laboratory parameters

assessed in women with PCOS

Parameter	Mean±SD	Range
FBS, mg/dl	100.83±32.38	59-297
TG, mg/dl	209.69±148.49	48-978
CHOL, mg/dl	163.03±47.45	46-264
HDL, mg/dl	35.94±11.14	14-68
LDL, mg/dl	89.82±30.79	13-151
HbA1c, %	5.18±0.87	3.8±9.6
Insulin, uIU/ml	13.69±12.17	2.5-83.4
TSH, µIU/ml	3.02±1.19	0.5-6.0
T4, µg/dl	7.22±1.81	1.7-14.0
T3, ng/ml	1.23±0.18	0.78-1.71
Cr, mg/dl	0.85±0.21	0.4-1.3

Thyroid function and its association with PCOS

Regarding the status of thyroid hormones in women with PCOS, the mean serum level of TSH was 3.02±1.19 µIU/ml, the mean level of T4 was 7.22±1.81 µg/dl and the mean level of T3 was 1.23±0.18 ng/ml. Based on the normal values of thyroid hormones, none of the PCOS patients had abnormal level of TSH and T3 hormones. Also, normal level of T4 was revealed in 90.8% of patients, while only 6.9% and 2.3% had T4 level lower than and higher than the normal range respectively. Using the correlation tests, none of the thyroid hormones was linearly associated with age, weight, BMI, the value of FBS or the levels of lipid profiles (Table 3).

Table 3. Association between thyroid hormones and other study parameters

Parameter	TSH, µIU/ml r (*P*)	T4, µg/dl r (*P*)	T3, ng/ml r (*P*)
Age, year	0.77 (0.479)	-0.094 (0.386)	0.000 (0.999)
BMI, kg/m^2	0.109 (0.315)	0.030 (0.782)	-0.114 (0.293)
FBS, mg/dl	-0.081 (0.454)	0.020 (0.854)	0.102 (0.348)
TG, mg/dl	-0.077 (0.477)	0.023 (0.835)	0.097 (0.370)
CHOL, mg/dl	0.103 (0.343)	-0.046 (0.673)	0.032 (0.770)
HDL, mg/dl	0.090 (0.407)	0.077 (0.481)	0.055 (0.614)
LDL, mg/dl	-0.010 (0.928)	-0.092 (0.395)	-0.027 (0.804)
HbA1c, %	0.053 (0.628)	0.069 (0.527)	0.065 (0.548)
Insulin, uIU/ml	-0.065 (0.553)	0.121 (0.264)	0.055 (0.613)
Cr, mg/dl	0.184 (0.088)	-0.168 (0.120)	-0.091 (0.401)

Discussion

Despite different pathophysiological pathways involved in PCOS and thyroid dysfunction, some recent evidence could show common patterns on autoimmunity, metabolic abnormalities, and hormonal changes in both disorders. However, the present study could not demonstrate a link between the patterns of abnormal hormonal changes of the thyroid in PCOS. Contrarily, a majority of those women suffered significant abnormalities in the lipid and glucose metabolisms. In other words, despite changes in thyroid hormones including TSH, T3, and T4 in normal ranges in almost all women with PCOS, hyperlipidemia, and hyperglycemia were prominent in a majority of those women. More interestingly, the high prevalence of overweight and obesity could emphasize high rate of adiposity and lipid pathways irregularities in such patients. It seems that the thyroid function in such women may be completely independent to glucose and lipid metabolic pathways at least in our population. Because of the controversies in the significant link between abnormal changes in thyroid hormones in PCOS patients, this association may be different in various ethnical conditions. As indicated by Singla *et al.*, on Indian women with PCOS (16), PCOS patients were found to have higher mean TSH level than that of the control group with also higher rate of goiter in the former group. Besides of probable ethnical effects, the discrepancy between our final result and their study was related to difference in age ranges in different populations, so that in Singla *et al*., study, the age group of PCOS is maximum in 15-20 years and has decreased significantly after 30 years, but in our study population, we have no women aged lower than 22 years and most of our patients aged higher than 30 years. The notable difference in our survey and the pointed study on Indian

women was the significant difference in the prevalence of obesity as 98% and 50% indicating clear difference in the metabolic background of PCOS in different populations. In another study on Chinese women with PCOS (17), the prevalence of AIT, serum TSH, anti-TPO and anti-Tg positive rate in PCOS patients are all significantly higher than those in control groups. Summing the study findings on the effect of age on the association between thyroid disease and PCOS shows different patterns of thyroid disorders in PCOS condition in different age subgroups. Although PCOS may be more found in younger ages in eastern population with high likelihood of simultaneous thyroid disturbances, PCOS may affect older women with a weak relation between thyroid disturbances and PCOS. In other words, the likelihood that a young woman with PCOS will have disease-causing hyperthyroidism particularly with the autoimmune background is very low in the general Western population (18).

According to present results regarding high prevalence of lipid metabolic disturbances in both PCOS and thyroid disorders, the pathophysiological link between these two diseases may be rooted in metabolic disorders related to obesity, lipid changes, and hormonal regulatory pathways of these conditions. As previously shown, although no correlations are suggested between the underlying causes of hypothyroidism and PCOS, these two diseases have many characteristics in common, such as chronic anovulation; decreased serum sex hormone binding globulin; and increased serum cholesterol and androgenic hormones (19).

In the current study, a small number of patients with PCOS had abnormal glycemic condition manifested by hyperglycemic state and raised hemoglobin A1C. In our study, only13.8% were hyperglycemic, and 21.8% of those had uncontrolled glycemic status. In fact, in our study population, insulin resistance might not have a central role in common pathogenesis between thyroid dysfunction and PCOS. As indicated in the literature, insulin resistance is a common mechanism in both PCOS and thyroid dysfunction leading to lipid and metabolism alteration. In some previous studies, it has been suggested a threshold of TSH to predict insulin resistance in women with PCOS, so those women with TSH higher than 2.5 mIU/l may have a significantly higher risk for altered insulin resistance (20). However, such cutoff values may not be applicable in all such as in Iranian population as shown in our survey.

It seems that our paradoxical results regarding the close link between altering thyroid hormones and PCOS may be significantly affected by racial factors and genetic tendency, however selecting women with higher mean age as well as high rate of obesity and overweight might confound the link between PCOS and thyroid problems and that should be adjusted in further assessment.

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