Research Article

The Prevalence of Clinical, Subclinical Hypothyroidism and Autoimmune Thyroiditis in patients with Polycystic Ovarian Syndrome

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Date Submitted: 25/2/2015
Date Accepted:17/6/2015

Abstract

Background: Abnormal thyroid function test is generally associated with polycystic ovarian syndrome (PCOS).

Objective: To detect the prevalence of hypothyroidism modalities in patients with PCOS and to evaluate the role of thyroid hormone changes in association with PCOS.

Study design and setting: A cross sectional study carried out at the Department of Gynecology and Obstetrics at Al-Yarmouk Teaching Hospital for a period of one year from January 2013 to January 2014.

Patients and Methods: One hundred females with polycystic ovarian syndrome were taken. From each patient, blood sample was taken for thyroid function test (triiodothyronine (T3), thyroxine (T4), thyroid stimulating hormone (TSH)), anti-thyroid antibodies (anti-thyroid peroxidase antibodies (anti TPO)) and anti-thyroglobulin antibodies (anti-TG).

Results: The current study revealed that the prevalence of thyroid dysfunction in the participant females with PCOS was 29% (9% had subclinical hypothyroidism, 5% had clinical hypothyroidism and 15% had autoimmune thyroiditis). Thyroid stimulating hormone had shown to be significantly higher ($p<0.001$) among the PCOS female group with thyroid dysfunction (being the highest in clinical hypothyroid, while it's increased level shows no significant difference between the subclinical hypothyroid group and autoimmune thyroiditis group) as compared to euthyroid females with PCOS. Higher levels of thyroid auto-antibodies were present in the sera of PCOS patients diagnosed with autoimmune thyroiditis (46.7%).

Conclusion: The current study showed that clinical, subclinical hypothyroidism and autoimmune thyroiditis were found in a significant number of patients with polycystic ovarian syndrome. We recommend assessment of the thyroid function routinely in patients with PCOS and offer thyroid hormone replacement therapy if necessary.

Key words: PCOS, thyroid hormones, thyroid auto-antibodies.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a common endocrinopathy affecting approximately 5–10% of women of reproductive age [(1)]. PCOS seems to be adversely affected by associated thyroid dysfunction, both pose independent risks of ovarian failure and pregnancy related complications [(2)]. Subclinical hypothyroidism (SCH) is defined as a serum thyroid-stimulating hormone (TSH) level above the upper limit

of normal despite normal levels of serum free thyroxine. Serum TSH has a log-linear relationship with circulating thyroid hormone levels (a 2-fold change in free thyroxine will produce a 100-fold change in TSH). Thus, serum TSH measurement is the necessary test for diagnosis of mild thyroid failure when the peripheral thyroid hormone levels are within normal laboratory range [3]. Severe hypothyroidism may be associated with diminished libido and failure of ovulation. Primary ovarian failure can also be seen in patients with Hashimoto's thyroiditis as a part of autoimmune polyglandular syndrome. Rarely, in primary hypothyroidism, secondary depression of pituitary function may lead to ovarian atrophy and amenorrhoea[4]. It is shown that hypothyroidism causes collagen deposition within the ovarian intracellular matrix. Increased collagenic material in the ovaries creates problems with ovarian function and may dysregulate hormone synthesis [5]. More interestingly hypothyroidism can initiate, maintain or worsen the PCOS[4]. Hence, in the past few years different studies from various parts of the world regarding thyroid disorders in PCOS patients have tried to explore the PCOS-thyroid interface. Mostly the results showed higher incidence of elevated TSH levels and four times higher prevalence of autoimmune thyroiditis in PCOS subjects [4]. On average, women with PCOS have higher TSH levels and are also more likely to have subclinical hypothyroidism when compared to age-matched controls without PCOS[6]. Interestingly, subclinical hypothyroidism caused insulin resistance in women with PCOS in all weight categories[7] . Thus we carried this study to find the relationship between PCOS and thyroid dysfunction.

PATIENTS AND METHODS

A cross-section observational study was carried out on a total of 100 women in the reproductive age period with polycystic ovarian syndrome collected from the infertility unit and outpatient clinic of the gynecological department of Al-Yarmouk Teaching Hospital; Baghdad, Iraq .The study was conducted over a period of one year, from January 2013 to January 2014. Verbal consent was obtained from all women participated in our study, inclusion criteria: the Rotterdam classification was used to define PCOS with two or more of these criteria: menstrual abnormalities, clinical and/or biochemical hyperandrogenism and ultrasound appearance of polycystic ovaries (multiple cysts >12 in number of 2-9 mm size)[8]. Exclusion criteria: other causes of hyperandrogenism like congenital adrenal hyperplasia, virilising tumor, Cushing syndrome and prolactinoma. Detailed history and examination had been done for all patients and investigations in form of ultrasound, blood glucose (fasting and 2 hrs post 75 g glucose), serum LH, FSH, free testosterone and prolactin measured by an automated immune-enzyme assay systems. Other causes of hyperandrogenism are excluded by ultrasound and urinary levels of corticosteroids. For detecting thyroid disorders: - thyroid stimulating hormone (TSH), free thyroxine (T4) and triiodothyronine(T3), anti-thyroperoxidase antibody (anti-TPO Ab) and anti-thyroglobulin antibody (anti-TG Ab) were estimated by using the commercially available VIDS Kits (Human IMTEC-Autoimmune diagnostics ELISA / Germany). All investigations were done at the laboratory of Al-Yarmouk Teaching Hospital and National Diabetic centre.

RESULT

Of the 100 women with polycystic ovarian syndrome studied; 71 (71%) were found to be euthyroid, 15 (15%) were diagnosed to have autoimmune thyroiditis (AITD), 9 (9%) were diagnosed to have SCH and only 5 (5%) presented with clinical hypothyroidism(CH). As shown in **figure 1**.

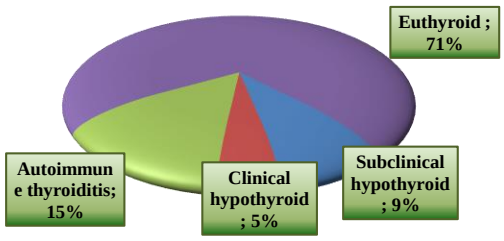

Figure 1. The prevalence of subclinical, clinical hypothyroidism and autoimmune thyroiditis in a sample of polycystic ovarian syndrome females, n=100.

Fifteen of studied women have had AITD. Anti- TPO Ab were detected in the sera of 5 (33.3%), anti-TG Ab were detected in 3 (20%) of them while both types of auto-antibodies were found in the sera of 7 (46.7%) as shown in figure (2).

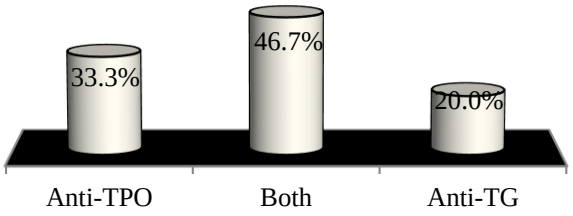

Figure 2. Types and percentages of thyroid auto-antibodies presented in the sera of PCOS patients diagnosed with AITD, n=15.

Table 1 below illustrates the average age and body mass indices of women with PCOS included in the study and according to their thyroid status. Despite the differences noted, none of them reaches the statistically significant level.

The results of the current study showed that no significant differences were found in the levels of fasting blood sugar, 2 hrs post 75 gm glucose test and hormonal parameters studied as shown in table 2 below.

Table 3 demonstrates the results of thyroid function test in females with polycystic ovarian syndrome.

Regarding thyroid stimulating hormone; the highest levels were detected in females with CH comparing to that in SCH and AITD, while the lowest level were found in the euthyroid group, these differences were statistically significant (p<0.001). Free serum thyroxin and triiodothyronine levels were also shown to be significantly different between the four groups (p<0.001, p=0.014), the lowest levels were in females with CH group while the levels in the other groups were somewhat close to each other with the highest level in euthyroid group.As studies demonstrated a significant relation of PCOS with TSH level [6,7,9,10], Table 4 demonstrates Tukey's post hoc test to clarify the relation of TSH level among the four groups. In CH group it was significantly higher than other groups (p<0.001), and its level in euthyroid group was significantly lower comparing to other groups (p<0.001), while it was insignificantly different between SCH and AITD groups. **Figure 3** below shows the significantly low level of free serum thyroxin and triiodothyronine levels in the females of clinical hypothyroid group comparing to other groups.

Table 1: Comparison of the age and body mass indices of PCOS females according to their thyroid status, n=100.

Variables	SCH (n=9) Mean±(SD)	CH (n=5) Mean±(SD)	AITD (n=15) Mean±(SD)	Euthyroid (n=71) Mean±(SD)	p-value¥
Age (years)	28±(5.3)	30±(6.8)	29±(4.8)	29±(6.8)	0.98 (NS)
BMI (kg/m^2)	28.7±(3.7)	30.1±(4.8)	27.6±(4.9)	28.6±(5.2)	0.79 (NS)

¥ANOVA test, SD=Standard deviation, BMI=body mass index, NS=Not significant.

Table 2: Comparison of the metabolic and hormonal parameters of PCOS females according to their thyroid status, n=100.

Variables	SCH (n=9) Mean±(SD)	CH (n=5) Mean±(SD)	AITD (n=15) Mean±(SD)	Euthyroid (n=71) Mean±(SD)	p-value¥
FBS (mg/dl)	92±(7.8)	93±(5.3)	89±(6.4)	94±(6.9)	0.085 (NS)
OGTT (mg/dl)	122±(12.3)	121±(12.6)	119±(14.1)	117±(12.6)	0.644 (NS)
LH (mIU/ml)	12.9±(5.3)	13.3±(4.1)	14.4±(4.9)	14.2±(5.1)	0.871 (NS)
FSH (mIU/ml)	5.6±(2.3)	6.0±(2.4)	6.9±(2.5)	6.4±(2.0)	0.519 (NS)
LH/FSH ratio	2.3±(1.4)	2.1±(1.3)	2.1±(1.5)	2.2±(1.8)	0.99 (NS)
Testosterone (pg/ml)	4.7±(1.5)	4.6±(1.4)	4.6±(1.4)	4.9±(1.6)	0.887 (NS)
Prolactin (ng/ml)	22.4±(7.5)	22.8±(7.7)	21.9±(7.1)	19.1±(11.3)	0.599 (NS)
Estradiol (pg/ml)	73.3±(3.2)	68.4±(6.3)	71.4±(3.7)	69.7±(6.1)	0.22 (NS)

¥ANOVA test, SD=Standard deviation, FBS=Fasting blood glucose, GTT= Glucose tolerance test, LH=Luteinizing hormone, FSH=Follicular stimulating hormone, NS=Not significant.

Table 3: The results of thyroid function test of PCOS females, n=100.

Variable	SCH (n=9) Mean±(SD)	CH (n=5) Mean±(SD)	AITD (n=15) Mean±(SD)	Euthyroid (n=71) Mean±(SD)	p-value
TSH (µU/mL)	6.8±(1.1)	19.6±(1.6)	6.5±(0.9)	2.1±(0.7)	<0.001*
FT4 (pmol/L)	11.1±(1.2)	6.3±(1.7)	10.9±(0.9)	11.6±(1.0)	<0.001*
FT3 (pmol/L)	4.6±(1.0)	2.9±(0.5)	4.6±(1.1)	4.7±(1.2)	0.014*

SD=Standard deviation, TSH=thyroid stimulating hormone, FT4=Free serum thyroxin, FT3=free serum triiodothyronine, * significant at α <0.05.

Table 4: Tukey's post-hoc test for comparison of the thyroid stimulating hormone mean levels between the different categories of thyroid status among PCOS females, n=100.

Thyroid stimulating hormone TSH (µU/mL)		Mean Differences	p-value
Euthyroid	Subclinical Hypothyroidism	-4.7	<0.001*
	Clinical hypothyroidism	-19.5	<0.001*
	Autoimmune thyroiditis	-4.3	<0.001*
Subclinical Hypothyroidism	Euthyroid	4.7	<0.001*
	Clinical hypothyroidism	-14.8	<0.001*
	Autoimmune thyroiditis	0.3	0.65(NS)
Clinical hypothyroidism	Euthyroid	19.5	<0.001*
	Subclinical Hypothyroid	14.8	<0.001*
	Autoimmune thyroiditis	15.1	<0.001*
Autoimmune thyroiditis	Euthyroid	4.3	<0.001*
	Subclinical Hypothyroidism	-0.3	0.65(NS)
	Clinical hypothyroidism	-15.1	<0.001*

NS=not significant, * significant at α <0.05.

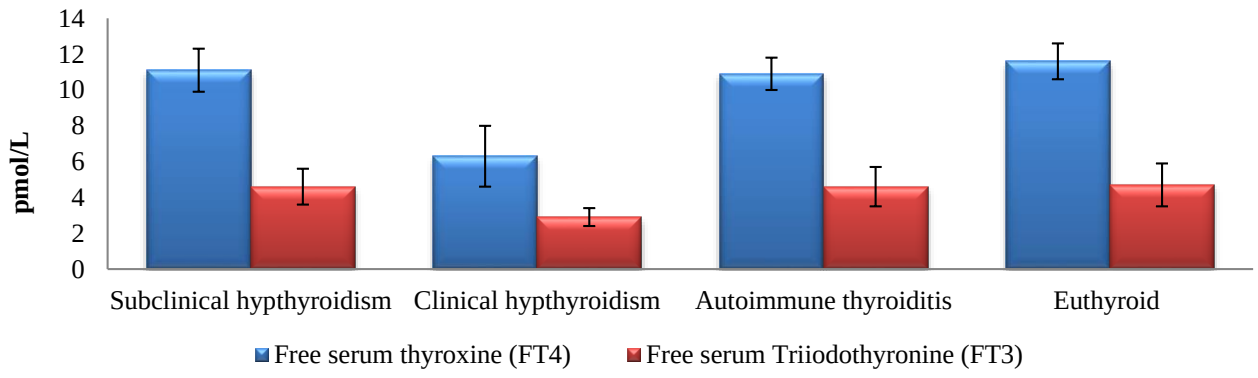

Figure 3: Comparison of the means and standard deviations of free serum (thyroxin and triiodothyronine) according to the thyroid status of women with PCOS, n=100.

DISCUSSION

It is evident that both hypothyroidism and PCOS have profound effects on fertility and reproductive biology. Many studies assess the relationship between PCOS and thyroid dysfunction, ***Janseen et al*;2004**[4] in Germany concluded that the prevalence of CH in PCOS females was very high (42.3%), TSH level in AITD group was significantly higher than euthyroid group, but the level of other hormones (free serum thyroxin and triiodothyronine) were not significantly different between the groups. ***Najem et al*; 2008**[11] in Libya reported that 3% of PCOS had AITD while ***Petrikova et al* ; 2010**[12] in Slovakia found that 19% of PCOS females were positive for thyroid antibodies. This difference in the prevalence of autoimmune thyroiditis between the current study and comparable studies might be due to the difference in the method of detecting autoimmune antibodies, sample size, ethnicity and geographic location. ***Al-Deresawi et al* ;2010-2011**[13] in Iraq reported that the prevalence of thyroid hormone dysfunction in their study sample was (20.8%), which was lower than that in our study (29%), this might be due to the difference in the setting of the studies, sample size and age ranges (they took older age groups as subjects were aged between 25 to 49 years in their study), in agreement with our study, they concluded that AITD is the most common form of thyroid dysfunction in PCOS females. ***Abd El-Hafez et al*;2013**[14] in Egypt reported that the thyroid dysfunction prevalence among PCOS patients was 25%, of them; only (7.5%) had CH. It also revealed that there were no differences between the thyroid dysfunction and euthyroid groups in the metabolic and hormonal features with specific changes for PCOS which is in the same line with our study. ***Garelli et al;2013***[15] in Italy found that thyroid dysfunction prevalence was 27% in patients with PCOS which was concurrent with our study. ***Sinha et al*; 2013**[2] in India revealed that hypothyroidism could

initiate, maintain or worsen PCOS and thereby correcting hypothyroid status in PCOS could improve the management. ***Benetti-Pinto et al;*****2013**[16] in Brazil showed a higher prevalence of SCH in young women with PCOS compared with that reported for the population of young women in general. ***Huang et al*****; 2014**[17] in China found that 14% of PCOS females had SCH. ***Enzevaei et al;*****2014**[18] in Iran revealed a high prevalence of SCH about 25.5% of total PCOS females. The last three studies were in agreement with our study as TSH was significantly higher in SCH compared to euthyroid group while free T3 and T4 didn't show any significant difference between the groups. ***Al-Saab and Haddad et al***; **2012**[19] in Syria, concluded a high prevalence of thyroid antibodies in euthyroid patients with PCOS. ***Ott et al*****; 2010**[20] in Austria found that 24% of PCOS were positive for anti-TG and anti-TPO antibodies. ***Kachuei's et al***;**2012**[21] in Iran showed a slightly higher prevalence of antibodies than that revealed in our results which might be due to the differences in the study component or the ethnicity of the patients as some areas are known to be highly affected by autoimmune diseases in comparison to other people. ***Karaköse et al***; **2013**[22] in Turkey concluded that Anti-TG was positive in (15%) of PCOS patients comparing to (20%) of PCOS patients with AITD in our study while in a study in ***Syria*** **2012**[19] found that (21.4%) of PCOS were positive to the anti-TG antibodies, while (28.6%) were positive to both types anti-TPO and anti-TG antibodies. These differences might be due to the fact that studies of incidence of autoimmune thyroid disease have only been conducted in a small number of developed countries [23], so the prevalence depends on the screening system of the country and its reliability to detect the antibodies as well as the educational health and willingness of the patients to attend the health facilities for the screening. Studies conducted in ***Romania*** in **2008** [24] and ***Syria*** **2012**[19] showed that TSH levels in AITD group were significantly higher than euthyroid group but the level of other hormones (free serum thyroxin and triiodothyronine) were not significantly different between the groups in patients with PCOS. Studies conducted in ***Syria*** in **2012**[19], ***Iran*** in **2012**[21] and ***Turkey*** in **2013**[25], also showed that there were no differences between the thyroid dysfunction groups and euthyroid groups in the androgenic, metabolic and hormonal features with specific changes for PCOS, which were in the same line of the findings of the current study. These differences in the prevalence of various thyroid dysfunctions between the current study and the comparable studies might be due to the heterogeneity of women samples included, differences in the designs of these studies, sample sizes, ethnicity and geographical locations, variable iodine nutrition levels in the populations studied and other factors which also might have unpredictable effect on the final results.

We conclude that CH, SCH and AITD are found in a significant number of patients with PCOS and we recommend assessment of the thyroid function routinely in patients with PCOS and offer thyroid hormone replacement therapy if necessary.

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