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Is there association between thyroid stimulating hormone levels and the four phenotypes in polycystic ovary syndrome?

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ABSTRACT

Objectives: The aim of this study was to determine whether the incidence of subclinical hypothyroidism (SCH) is higher in polycystic ovary syndrome (PCOS) group than the control group. Additionally, the study investigated whether serum thyroid stimulating hormone (TSH) level is associated with various clinical parameters of PCOS regarding different phenotypes of the disease.

Material and methods: This retrospective, case-control study included 329 PCOS patients and 162 control women who were aged between 20 and 42 years and visited the Gynecology outpatient clinic in Pusan National University Hospital from January 2014 to December 2017. PCOS patients were further classified according to their phenotypes: phenotype A as the combination of all hyperandrogenism (HA), ovulatory dysfunction (OD), and polycystic ovarian morphology (PCOM); phenotype B as the combination of HA and OD; phenotype C as the combination of HA and PCOM; and finally, phenotype D as the combination of OD and PCOM. Laboratory blood tests included follicle stimulating hormone (FSH), luteinizing hormone (LH), TSH and anti-mullerian hormone (AMH). The ovarian volume was calculated using three diameters by gynecologic ultrasonography.

Results: Serum TSH level was significantly higher in PCOS patients than in the control group after adjusting for age and body mass index (BMI). Serum TSH level was not related to HA and OD, but its significant association with PCOM was confirmed in comparative analysis in quartiles. The proportion of phenotype A patients increased as serum TSH level increased, while the proportion of phenotype B and D decreased. Phenotype C stayed relatively consistent with varying TSH levels.

Conclusions: More numbers of patients showed elevated TSH level satisfying SCH diagnosis in PCOS group than the control group. In addition, a significant correlation between serum TSH level and different PCOS phenotypes has been observed; especially, PCOS patients with phenotype A, which displays all of HA, OD, and PCOM, tended to have the higher TSH levels than the PCOS patients with other phenotypes, requiring proper and thorough evaluation for potential endocrine disparity and according to management in such patient group.

Key words: PCOS; phenotypes; subclinical hypothyroidism; TSH

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in reproductive women, characterized by chronic ovulatory dysfunction (OD), clinical and/or biochemical signs of hyperandrogenism (HA), and/or ultrasound characteristics for polycystic ovarian morphology (PCOM) [1]. Accordingly, PCOS can exhibit clinical features such as infertility, hirsutism, weight gain, central obesity and acanthosis nigricans [2–4]. Pathologic hormonal profile of the disease includes elevated luteinizing hormone (LH) levels with normal or slightly decreased levels

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of follicle-stimulating hormone (FSH), hyperandrogenemia, and hyperinsulinemia [5].

Among such disturbed metabolic pathways underlying PCOS, insulin resistance appears to be the major etiological characteristic in most patients [6–8]. In women with PCOS, approximately 50–70% of the patients have been reported to have insulin resistance and metabolic syndrome [9–12]. Similar features are seen in patients with hypothyroidism; the patients with hypothyroidism may present with menstrual disorders, infertility, signs of hyperandrogenism, weight gain, dyslipidemia and insulin resistance [13, 14]. Regarding the thyroid function of PCOS patients, Yu and Wang have concluded that PCOS is associated with the higher incidence of subclinical hypothyroidism (SCH) compared to the normal population [13]. SCH, defined as an elevated thyroid-stimulating hormone (TSH) level with normal thyroid hormone levels and lack of signs or symptoms of hypothyroidism, also results in these features [10, 15]. The prevalence of SCH in women with PCOS is variable, ranging from 11 to 36% [16, 17]. Pathophysiological connection between the two disorders has not been established until now; yet, Singla et al. suggest that multiple factors, including adiposity, increased insulin resistance, high leptin and evidence of deranged autoimmunity, contribute individually and interconnectedly to both of SCH and PCOS [18].

Composing such complicatedly mixed endocrine abnormalities within the disease, PCOS patients present diverse clinical characteristics and phenotypes. As an attempt to facilitate the understanding of the disease in both research purpose and clinical setting, the NIH consensus panel recommended four types of phenotype classification in PCOS as a systematic effort: phenotype A as the combination of all HA, clinical or biochemical presence, OD and PCOM; phenotype B as the combination of HA and OD; phenotype C as the combination of HA and PCOM; and finally, phenotype D as the combination of OD and PCOM [19]. Previous literature has thoroughly explored the significant relationship between serum TSH level and PCOS itself; however, as far as we know, only a limited number of studies have discussed the association between TSH and specific PCOS phenotypes [20, 21]. Thus, it is necessary to compare the possibly different association of each PCOS phenotype and TSH in pursue of providing patients with more individualized, efficient therapeutic and disease management plan.

Objectives

in this study, serum TSH levels of the PCOS patients and control were first compared to determine whether the incidence of SCH is higher in PCOS group. Next, the study investigates the possible, significant association of TSH level in PCOS patients with their clinical parameters and PCOS phenotypes.

MATERIAL AND METHODS

Patients and diagnostic criteria of PCOS

This study was a retrospective, case-control study, analyzing electronically charted patient records of the Gynecology outpatient clinic in Pusan National University Hospital. The study included a total of 329 patients, composed of 162 patients in the control group and 167 patients in PCOS group with the age group of 20 to 42 years, who visited the clinic between January 2014 and December 2017. All patients in this study were non-smokers, were not indicated with levotyroxin supplementation and had never taken hormonal contraceptives and/or analgesics at the time of patient selection. Those patients with underlying diseases regarding thyroid or pituitary, abnormal autoimmune antibody levels and/or thyroid ultrasonographic findings, TSH level out of reference range (0.25–5.0 mIU/L) and other related disorders such as congenital adrenal hyperplasia (CAH), Cushing's syndrome or virilizing tumors were excluded [1, 22, 23].

PCOS diagnosis was based on revised 2003 Rotterdam criteria, which confirms PCOS when the patient presents with two out of the following three features: first, OD represented as abnormal menstrual cycle such as amenorrhea, which was defined as the absence of menstrual cycles in the last six months, or oligomenorrhea, which was defined as having the cycle interval of 35 days or more; second, clinical HA, such as hirsutism, alopecia and/or acne or biochemical HA of serum testosterone higher than 2.0 nmol/L; last, the presence of PCOM on gynecologic ultrasonography, showing 12 or more follicles with 2 to 9 mm in diameter and/or ovarian volume of larger than 10 cm^3 on either ovary. Each presentation of clinical HA was determined using previously established diagnostic criteria — for hirsutism, modified Ferriman Gallway score with cut-off score of ≥ 6; for alopecia, the Ludwig visual score; and for acne, despite the absence of universal agreement on visual assessments for its evaluation, the term "acne vulgaris" (AV**)** applied when the patient had a pilosebaceous unit that causes noninflammatory comedones, inflammatory lesion containing red papules, pustules or nodules, and varying degrees of scarring [24–26]. The diagnosed PCOS patients were further categorized into four groups according to their phenotypes: phenotype A as the combination of all HA, OD, and PCOM; phenotype B as the combination of HA and OD; phenotype C as the combination of HA and PCOM; and finally, phenotype D as the combination of OD and PCOM [19].

The control group included age-matched healthy women without any of HA, OD or PCOM who had performed blood thyroid function test (TFT) for other non-related surgical indications such as ovarian endometrioma, mature cystic teratoma and/or cystadenoma.

Table 1. Comparative description of FSH, LH, ovarian volume and clinical presentations of PCOS patients according to the varying ranges of serum TSH levels

		Overall (n = 167)	TSH < 2.0 (n = 76)	2.0 ≤ TSH < 4.5 (n = 77)	TSH ≥ 4.5 (n = 14)	p value
FSH[a] [mIU/mL]		6.21 ± 2.35	5.99 ± 2.53	6.48 ± 2.26	5.92 ± 1.67	0.394
LH[b] [mIU/mL]		6.52 [3.68, 10.16]	6.17 [2.47, 10.43]	6.58 [4.11, 9.79]	6.12 [4.81, 7.95]	0.887†
LH:FSH ratio[b]		1.11 [0.64, 1.57]	1.13 [0.59, 1.69]	1.08 [0.64, 1.56]	1.07 [0.67, 1.25]	0.914†
Ovarian volume[a] [cm^3]		13.57 ± 16.84	11.29 ± 15.12	14.32 ± 17.50	21.83 ± 20.13	0.085
Clinical presentations[a]						
HA (%)	No	66 (39.5)	35 (46.1)	29 (37.7)	2 (14.3)	0.074
	Yes	101 (60.5)	41 (53.9)	48 (62.3)	12 (85.7)	
OD (%)	No	4 (2.4)	2 (2.6)	2 (2.6)	0 (0.0)	1.000‡
	Yes	163 (97.6)	74 (97.4)	75 (97.4)	14 (100.0)	
PCOM (%)	No	36 (21.6)	20 (26.3)	14 (18.2)	2 (14.3)	0.829
	Yes	131 (78.4)	56 (73.7)	63 (81.8)	12 (85.7)	
Phenotypes[a] (%)						
A: HA-OD-PCOM		61 (36.5)	19 (25.0)	32 (41.6)	10 (71.4)	0.039*/+0.004‡
B: HA-OD		36 (21.6)	20 (26.3)	14 (18.2)	2 (14.3)	
C: HA-PCOM		4 (2.4)	2 (2.6)	2 (2.6)	0 (0.0)	
D: OD-PCOM		66 (39.5)	35 (46.1)	29 (37.7)	2 (14.3)	

[a]Data are presented at the means ± SD; [b]data are presented at the median [IQR]; independent t-test or Wilcoxon rank-sum test(†) was used for continuous variable; Fisher's exact test(‡) was used for categorical variable. +p value for trend; *p < 0.05 was considered significant; FSH — follicle stimulation hormone; HA — hyperandrogenism; LH — luteinizing hormone; OD — ovulatory dysfunction; PCOM — polycystic ovarian morphology; TSH — thyroid stimulating hormone

Measurement of laboratory tests and ovarian volume

Laboratory blood tests were performed with the venous blood sampling at the time of PCOS diagnosis, and the tests included following measurements: FSH and LH using Dream Gamma-10 radioimmunoassay (RIA) (Shin Jin Medics Inc., Korea) of which measurements were used to calculate LH/FSH ratio; TSH using Coat-A-count TSH IRMA Kit (SIMENS, Ireland); and anti-mullerian hormone (AMH) using an Anti-Mullerian Hormone/Mullerian Inhibiting Substance Enzyme Immuno Assay (AMH/MIS EIA) kit (Beckman Coulter, France). Body mass index (BMI) was calculated as the patient's weight in kilograms divided by her height in meters squared. All PCOS patients underwent transvaginal or transrectal ultrasonography to determine the volume of both ovaries and the size of ovarian follicles using a 5–9 MHz transvaginal transducer or transrectally for virgin patients (Voluson E6 General Electric, Milwaukee, Wauwatosa, WI, USA). The ovarian volume was calculated using the longest longitudinal (d1), anteroposterior (d2), and transversal diameters (d3): volume in cm^3 = d1 x d2 x d3 x 0.523. Patients were examined at a random day during the menstrual cycle because ultrasonography was performed on the first day of their visit to the hospital.

Arbitrarily, the related factors were identified by dividing the TSH levels into three groups according to their range: TSH < 2, 2.0 ≤ TSH < 4.5, TSH ≥ 4.5. The total volumes of ovaries, FSH and LH were found to be unrelated (Tab. 1). Since the patients were divided randomly only according to their TSH levels, as shown in Table 1, distribution of the number of subjects in each group was uneven. As a result, the possible factors related to the uneven distribution of the patients which could have influenced the results of the study were evaluated by dividing the total number of subjects in quartiles based on TSH level, as described in Table 2: 0.11 ≤ quartile 1 < 1.40; 1.40 ≤ quartile 2 < 2.14; 2.14 ≤ quartile 3 < 3.41; and 3.41 ≤ quartile 4 ≤ 6.86.

Statistical analysis

Data were analyzed according to their patterns of distribution using parametric or nonparametric test. Continuous variables were expressed as mean ± SDs, and categorical variables as numbers and percentages. When comparing the two groups as in Tables 1 and 3, independent t-test or Wilcoxon rank-sum test was used to assess the continuous variable, and Chi-square test or Fisher's exact test was used to assess the categorical variable. As shown in Table 4, one-way ANOVA or Kruskal-Wallis test was performed for comparing multiple groups. The logistic regression analysis was performed to assess the effect of various factors on PCOS. In multivariable analysis, factors with the potential to affect PCOS — age and BMI — were adjusted and included

Table 2. Comparative description of FSH, LH, ovarian volume and clinical presentations of PCOS patients according to the quartiles of serum TSH level

	Overall	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p value
	(n = 167)	(n = 42)	(n = 42)	(n = 42)	(n = 41)	
FSH[a] [mIU/mL]	6.21 ± 2.35	6.18 ± 2.62	5.77 ± 2.53	6.55 ± 2.35	6.34 ± 1.81	0.489
LH[b] [mIU/mL]	6.52 [3.68, 10.16]	5.78 [2.30, 10.29]	6.88 [4.18, 10.99]	7.26 [4.28, 9.65]	5.47 [4.09, 8.67]	0.755†
LH:FSH ratio[b]	1.11 [0.64, 1.57]	1.00 [0.55, 1.64]	1.25 [0.80, 2.12]	1.20 [0.62, 1.48]	0.82 [0.67, 1.24]	0.245†
Ovarian volume[a] [cm^3]	13.57 ± 16.84	12.95 ± 15.73	10.85 ± 15.06	14.99 ± 17.92	15.53 ± 18.65	0.574
Clinical presentations[a]						
HA (%)	66 (39.5)	17 (40.5)	21 (50.0)	11 (26.2)	17 (41.5)	0.162
	101 (60.5)	25 (59.5)	21 (50.0)	31 (73.8)	24 (58.5)	
OD (%)	4 (2.4)	1 (2.4)	1 (2.4)	1 (2.4)	1 (2.4)	1.000‡
	163 (97.6)	41 (97.6)	41 (97.6)	41 (97.6)	40 (97.6)	
PCOM (%)	36 (21.6)	16 (38.1)	6 (14.3)	9 (21.4)	5 (12.2)	0.017*
	131 (78.4)	26 (61.9)	36 (85.7)	33 (78.6)	36 (87.8)	
Phenotypes[a] (%)						
A: HA-OD-PCOM	61 (36.5)	8 (19.0)	14 (33.3)	21 (50.0)	18 (43.9)	0.022*/+0.148‡
B: HA-OD	36 (21.6)	16 (38.1)	6 (14.3)	9 (21.4)	5 (12.2)	
C: HA-PCOM	4 (2.4)	1 (2.4)	1 (2.4)	1 (2.4)	1 (2.4)	
D: OD-PCOM	66 (39.5)	17 (40.5)	21 (50.0)	11 (26.2)	17 (41.5)	
TSH quaternary						
	0%	25%	50%	75%	100%	
	0.11	1.40	2.14	3.41	6.86	

[a]Data are presented at the means ± SD; [b]Data are presented at the median [IQR]; One-way ANOVA or Kruskal-Wallis test(†) for continuous variable; Chi-square test or Fisher's exact test(‡) for categorical variable; +p value for trend; *p < 0.05 was considered significant; FSH — follicle stimulation hormone; LH — luteinizing hormone; HA — hyperandrogenism; OD — ovulatory dysfunction; PCOM — polycystic ovarian morphology; TSH — thyroid stimulating hormone

Table 3. Characteristics of the study population

	Overall (n = 329)	PCOS (n = 167)	Control (n = 162)	p value
Age (years)	27.43 ± 6.16	25.38 ± 4.98	29.55 ± 6.55	< 0.001*
BMI [kg/m^2]	22.33 ± 4.50	22.75 ± 4.57	21.91 ± 4.39	0.088
AMH [ng/mL]	7.43 ± 5.81	11.19 ± 5.60	3.55 ± 2.60	< 0.001*
TSH [mIU/mL]	2.27 ± 1.23	2.39 ± 1.34	2.15 ± 1.09	0.085

Data are presented at the means ± SD. *p < 0.05 was considered significant.; AMH — anti-Mullerian-hormone; BMI — body mass index; PCOS — polycystic ovary syndrome; TSH — thyroid stimulating hormone.

TSH. All statistical analyses were conducted using R 4.0.1., and p value < 0.05 was considered statistically significant.

RESULTS

Table 3 features the basic characteristic of the patients included in the study. The mean age of the study population was 25.38 ± 4.98 years in the PCOS group and 29.55 ± 6.55 years in the control group (described as means ± standard deviation [SD], p < 0.001). BMI was not statistically different in overall patients, with mean ± SD of 22.33 ± 4.50 kg/m^2. As observed in previous literature, AMH level of the PCOS group was statistically higher than the control group which included patients with benign ovarian cysts such as endometrioma, mature teratoma and/or cystadenoma (11.19 ± 5.60 ng/mL in the PCOS group and 3.55 ± 2.60 in the control group, described as means ± SD with p < 0.001, respectively) [27].

Logistic regression analysis, adjusted for age and BMI, was performed to compare TSH levels between the control and PCOS groups, as described in Table 4. Multivariable analysis showed that TSH level was significantly higher in the PCOS group compared to the control group, with odds ratio (OR) of 1.226 and 95% confidence interval (CI) of 1.006, 1.493 (p < 0.05). In the univariable analysis, the comparison

Table 4. Logistic regression analysis of patient characteristics for PCOS diagnosis including varying ranges of TSH levels, adjusted for age and BMI

	Univariable analysis		Multivariable analysis	
	OR [95% CI]	p value	OR [95% CI]	p value
Age [years]	0.884 [0.848, 0.921]	< 0.001*	0.878 [0.841, 0.916]	< 0.001*
BMI [kg/m^2]	1.044 [0.993, 1.096]	0.090	1.049 [0.995, 1.106]	0.075
AMH [ng/mL]	1.762 [1.555, 1.997]	< 0.001*		
TSH [mIU/mL]	1.170 [0.978, 1.400]	0.087	1.226 [1.006, 1.493]	0.043*
< 2 (%)	Reference value			
2–4.5 (%)	1.196 [0.766, 1.868]	0.431		
≥ 4.5 (%)	3.132 [1.077, 9.102]	0.036*		

*p < 0.05 was considered significant; AMH — anti-Mullerian-hormone; BMI — body mass index; CI — confidence interval; OR — odds ratio; TSH — thyroid stimulating hormone.

of TSH levels was performed using the randomly divided three groups according to their range. The analysis showed that groups with TSH levels of 4.5 mIU/mL or higher had significantly higher rates of PCOS than those with TSH levels of less than 2 mIU/mL [OR (95% CI) of 3.132 (1.077, 9.102), p < 0.05].

As represented by Table 1, FSH, LH, LH:FSH ratio and the ovarian volumes of PCOS patients were not significantly associated with the varying ranges of their serum TSH levels. Also, regarding their clinical presentations, the results confirmed that serum TSH level was not specifically related to each of HA, OD and PCOM. However, significant relationships between the four types of PCOS phenotype and TSH have been identified (p < 0.05). As TSH level increased, the proportion occupied by phenotype A increased, while the proportion occupied by phenotype B decreased. Phenotype C stayed similar, and phenotype D also decreased with the increasing TSH level (p value for trend < 0.05).

According to Table 2, FSH, LH, LH:FSH ratio and the volumes of ovaries did not display significant relationship with the different quartiles of serum TSH levels, but PCOM did (p < 0.05). In addition, significant relationships between TSH level quartiles and different PCOS phenotypes were identified; however, unlike in Table 1 with varying ranges of TSH levels, the analysis did not observe a statistically significant trend (p = 0.148).

DISCUSSION

Over the decades, many studies have investigated the prevalence of SCH in PCOS. Consequently, it has been observed that PCOS and SCH are closely related, with thoroughly examined underlying mechanisms. However, only a few studies have been evaluated the relationship between TSH level and each different phenotype in patients with PCOS. To our knowledge, this is the first analysis to evaluate the relationship and its trends between the patient's TSH level and PCOS phenotype.

In order to evaluate such relationship, general characteristics of the overall patients – both PCOS and control – were first investigated. As one of the important biomarkers for ovarian function and reserve, serum AMH levels of the patients were routinely measured to evaluate their general and clinical characteristics when diagnosis in the PCOS group or planning for surgical treatments in the control group was made. As previously established, the current study observed significantly increased AMH level in PCOS patients compared to the control group [27]. It has been reported that elevated TSH could be associated with decreased AMH in infertile women, but those women were without PCOS or ovary-related surgical histories, which does not apply to the scope of the current study [28]. Moreover, the control group of the current study included patients with benign ovarian tumors such as endometriosis, mature cystic teratoma and/or cystademona; serum AMH levels among these patients with such various ovarian pathologies were diverse and all equally included in the statistical analysis, which resulted in 3.55 ± 2.60 ng/mL (mean ± SD). Such approach could have possibly nullified the possibly decreased AMH level of included endometriosis patients. Another important biomarkers for PCOS include serum LH, FSH and LH:FSH; especially, LH:FSH ratio has been known to be significantly different between the general population and PCOS patients [29]. In the current study, only those PCOS patients were evaluated for LH, FSH and LH:FSH ratio, and the results showed no significant differences in LH, FSH and LH:FSH ratio according to varying TSH levels, agreeing with the previous study of Cai et al. [30]. Lastly, BMI was evaluated as it could have possibly affected the physiologic status of the patients, and BMI was not significantly different between the control and PCOS patients, all lower than 25 kg/m^2. Generally speaking, the prevalence of obesity in PCOS women has been reported to be 30–75%, according to varying ethnicities [31]. Although a majority of PCOS patients are obese or overweight, a small but significant proportion of PCOS patients, termed with "lean" PCOS patients, do present with normal BMI, requiring different

therapeutic approach [32]. When comparing Asian and Caucasian PCOS patients, it has been reported that the Caucasian patients had a statistically greater increase in obesity prevalence than their Asian counterparts [33]. In the current study of Korean PCOS patients, it was not completely surprising to see that the included patients with Korean ethnicities had BMI lower than 25 kg/m^2. Moreover, as LH:FSH ratio dose not differ between obese and lean PCOS patients, the possible influence that lean status of PCOS patients in this study might have exerted on their TSH levels could have been minimal [34].

According to the current study, adjusting for age and BMI resulted in higher TSH levels in PCOS patients compared to the control group, as shown in Table 4. Similar results have been found in many other studies on the close relationship between PCOS and SCH. In the study by Qun Yu et al., in China, 27% of their PCOS patients had comorbid SCH, whereas only 8% of the control group did so [35]. Furthermore, the current study investigated whether such comorbidity was differently associated with TSH according to the PCOS features. In previous literature, Jie Cai et al. reported that the increased prevalence of HA was associated with the higher TSH level than other features, independent of age, BMI and thyroid autoimmunity in euthyroid PCOS patients [30]. On the other hand, according to the results of this study, the association between TSH and PCOS features such as HA, OD and PCOM was not statistically confirmed ($p = 0.074$). Other than the small number of patients included in this study, possible explanations include inevitable recall bias since the decision of OD was dominantly based on the patient's memory; in fact, the most common chief complaint of PCOS patients at the research facility was irregular menstruation. In addition, no significant difference in the PCOM prevalence was observed ($p = 0.829$).

However, the proportion of each phenotype turned out to be closely related to TSH according to the study; the higher the TSH level was, the higher the percentage of phenotype A in HA, OD and PCOM. Conversely, phenotype B, which represented HA and OD, decreased with higher TSH level. Phenotype C, representing HA and PCOM, was restrictively difficult to compare because the number of subjects was only four; in case of phenotype D, representing OD and PCOM, showed rather smaller percentage with the higher TSH level. In the group of PCOS patients with TSH level of 4.5 or higher, 71.4% showed phenotype A. Hence, it could be logically interpreted that when the TSH level increased, the probability of occurrence of all HA, OD and PCOM also increased, probably suggesting the pathophysiology between thyroid hormones and androgen played an important, causal role. As previously known, GnRH regulates the biosynthesis and secretion of LH and FSH, which are usually upregulated in PCOS; it is assumed that such GnRH could have modulated thyroid hormones at the pituitary level [30]. Indeed, there is evidence that thyroid hormones are involved in gonadal differentiation and reproductive function [36]. Thyroid hormones regulate androgen biosynthesis and signaling through direct and indirect regulation of the expression and activity of associated steroidogenic enzymes [37, 38].

Further investigating the association of TSH with PCOS features, Table 2 describes the total number of subjects divided in quartiles based on TSH level, showing somewhat slightly different results from Table 1; there was no significant difference in HA for each group, but PCOM was significantly different among the quartiles ($p = 0.017$). As in Table 1, there was a significant difference in phenotypes ($p = 0.022$), but, in Table 2, it was unreasonable to interpret that it had a certain tendency depending on the TSH level (p value for trend = 0.148). Despite that the same patient group was investigated, the reason for different results between Tables 1 and 2 could have been that in Table 2 the classification of the patient group was based on quartiles; the number of patients in each group was similarly distributed, but the range of their TSH levels were significantly different from each other. Therefore, according to the current study, it could be presumed that the TSH levels of 2.0 and 4.5 are statistically meaningful.

The current study still has several limitations. First, due to the retrospective nature of the current study, no useable data could have been newly obtained from the study population. Consequently, certain biochemical markers for HA were missing for example, sex hormone binding globulin (SHBG) and dehydroepiandrosterone (DHEA), as SHBG and DHEA measurements were limited due to the National Insurance Coverage restrictions in some cases. Instead, serum testosterone levels were measured to satisfy biochemical presentation of HA when a patient did not fulfill previously established diagnostic criteria but had symptoms of highly suggestive HA [24–26]. Last but importantly, as previously mentioned, the number of subjects included in the study was relatively small. Subgroups were divided based on TSH level, but the total number of subgroups with high TSH level was too small, possibly limiting the thorough analysis of the results. Further studies with prospective nature and larger population to strengthen the regarding statistical analysis of data character are required.

CONCLUSIONS

In conclusion, the current study confirmed higher prevalence of SCH in PCOS patients compare to the control group, and in such PCOS patients, the significant correlation between serum TSH level and specific PCOS phenotype was observed, with statistically confirmed tendency of elevating TSH level in increasing proportion of PCOS phenotype

A which included all of HA, OD and PCOM. Proper screening and patient guidance considering the hormonal status and phenotype of the patient at the same time could substantially accommodate clinicians to provide PCOS patients with more individualized, efficient therapeutic and management planning in clinical setting.

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None.

Conflict of interest

All authors declare no conflict of interest.

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