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Association between PCOS and autoimmune thyroid disease: a systematic review and meta-analysis

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Abstract

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disorder affecting women of reproductive age. PCOS has been associated with distinct metabolic and cardiovascular diseases and with autoimmune conditions, predominantly autoimmune thyroid disease (AITD). AITD has been reported in 18–40% of PCOS women, depending on PCOS diagnostic criteria and ethnicity. The aim of this systematic review and meta-analysis was to summarize the available evidence regarding the likelihood of women with PCOS also having AITD in comparison to a reference group of non-PCOS women. We systematically searched EMBASE and MEDLINE for non-interventional case control, cross-sectional or cohort studies published until August 2017. The Ottawa–Newcastle Scale was used to assess the methodological quality of studies. Statistical meta-analysis was performed with R. Thirteen studies were selected for the present analysis, including 1210 women diagnosed with PCOS and 987 healthy controls. AITD was observed in 26.03 and 9.72% of PCOS and control groups respectively. A significant association was detected between PCOS and chance of AITD (OR=3.27, 95% CI 2.32–4.63). Notably, after geographical stratification, the higher risk of AITD in PCOS women persisted for Asians (OR=4.56, 95% CI 2.47–8.43), Europeans (OR=3.27, 95% CI 2.07–5.15) and South Americans (OR=1.86, 95% CI 1.05–3.29). AITD is a frequent condition in PCOS patients and might affect thyroid function. Thus, screening for thyroid function and thyroid-specific autoantibodies should be considered in patients with PCOS even in the absence of overt symptoms. This systematic review and meta-analysis is registered in PROSPERO under number CRD42017079676.

Key Words

- ▶ PCOS
- ▶ autoimmune thyroid disease
- ▶ TSH
- ▶ systematic review
- ▶ meta-analysis

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Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disorder affecting women of reproductive age. The worldwide prevalence of PCOS ranges from 9 to 19.9%, depending on population characteristics and diagnostic criteria (1, 2, 3, 4, 5). Diagnosis of this complex multifactorial

disease is based on the presence of two out of three of the following: clinical and/or biochemical androgen excess, anovulation and polycystic ovaries on pelvic ultrasound. The mechanisms underlying individual susceptibility to PCOS include hyperinsulinemia, disruption of the

hypothalamic–pituitary–gonadal axis, dysregulation of ovarian steroidogenesis, low-grade chronic inflammation (6) and genetic and environmental factors (7, 8, 9). PCOS has also been associated with type 2 diabetes, insulin resistance, obesity, dyslipidemia, hypertension and metabolic syndrome, suggesting a contribution of the syndrome to cardiovascular risk (10, 11, 12, 13, 14, 15).

The association between inflammation and autoimmunity in women with PCOS has been extensively discussed in recent years (16). Chronic low-grade inflammation might be a relevant connecting link between obesity and metabolic manifestations in PCOS (6, 17). After detecting antiovarian autoantibodies localized to the granulosa cells in women with PCOS, Van Gelderen *et al.* suggested a role of stimulating ovarian antibodies in PCOS pathophysiology (18). However, the concept of an autoimmune etiology is not supported by other studies describing similar prevalence of antiovarian autoantibodies in women with PCOS and controls (19), leading to the proposal of systemic immune activation by nonorgan-specific autoantibodies in PCOS (20). This could explain the recurrent association between PCOS and autoimmune diseases (21, 22) and especially autoimmune thyroid diseases (AITD), the most common form of autoimmune disorder, with an estimated prevalence of 5% (23, 24, 25).

AITD results from a dysregulation of the immune system that produces an immune attack with consequent chronic inflammation of the thyroid gland. It is classified as a T cell-mediated organ-specific autoimmune disorder (26). Affected individuals are usually positive for thyroid peroxidase (TPOAbs) and/or thyroglobulin (TgAbs) antibodies, with a typical hypoechogenic pattern at ultrasonography (27, 28). AITD is regarded as the most frequent cause of hypothyroidism in young women. Nevertheless, detectable antibodies may be observed for years without overt thyroid dysfunction. Hence, AITD often goes unnoticed until the onset of hypothyroidism later in life (29). Furthermore, a recent meta-analysis has demonstrated that the presence of subclinical hypothyroidism in PCOS women produces mild metabolic abnormalities, affecting the levels of high-density lipoprotein (HDL), triglyceride and homeostatic model assessment for insulin resistance (HOMA-IR) (30).

To date, several studies evaluating the association between AITD and PCOS have been published without reaching a clear conclusion. A previous meta-analysis assessed the relationship between PCOS and some of its features and thyroiditis. That article included six studies, three of which were meta-analyzed to assess the

prevalence of thyroiditis among women with PCOS. The results suggested a higher incidence of thyroiditis in PCOS than those in controls (31). Therefore, the aim of this systematic review and meta-analysis was to summarize and update the available evidence regarding the likelihood of women with PCOS also having AITD in comparison to a reference group of women without PCOS.

Methods

Search strategy and study selection

EMBASE and MEDLINE databases were searched for studies published until August 2017. No other limits except for the end date were established for the search. The protocol for this systematic review and meta-analysis is registered in PROSPERO (<http://www.crd.york.ac.uk/PROSPERO/>) under number CRD42017079676. Medical subject headings (MeSH) used in the search are presented as supplementary data (see section on [supplementary data](#) given at the end of this article).

The research question was developed using the PICOS strategy: the population (P) was defined as women in menopause; the intervention (I) was defined as diagnosis of PCOS; the comparison group (C) corresponded to women without PCOS; the outcome (O) was defined as autoimmune thyroid disease (AITD) and the study design (S) was defined to include non-interventional case control, cross-sectional or cohort studies. This review had no year or language restrictions.

In case multiple reports of the same study were identified, the most complete report was chosen. If the abstracts did not provide enough information about inclusion and exclusion criteria, the full text was retrieved for evaluation.

Data extraction and quality control

Two investigators (M R and V C F) independently reviewed the titles and abstracts of all articles identified in the initial search to assess eligibility of the studies for inclusion in this systematic review and meta-analysis. The selected articles were read in full for confirmation of eligibility and data extraction. In case of disagreement, a third reviewer (P M S) was consulted. The following information was extracted from each study: name of first author, publication year, country, number of subjects in case and control groups, age, BMI and number of patients with AITD (according to the diagnostic criteria for AITD

described in the study) and serum levels of thyroid-stimulating hormone (TSH).

The Newcastle–Ottawa Scale (NOS) (Retrieved August, 2017, from: www.ohri.ca/programs/clinical_epidemiology/oxford.asp) was used to assess the quality of the studies included in the meta-analysis. The NOS uses a ‘star system’ to judge the included studies in three broad perspectives: selection of the study groups, comparability of those groups and ascertainment of outcome of interest.

Statistical analysis

Odds ratios (ORs) were used to measure the association between diagnostic status (PCOS or healthy) and AITD. ORs were pooled by the Mantel and Haenszel method using a random effects model with Der Simonian and Laird’s estimator. The Mantel–Haenszel method is more appropriate when using OR because it provides interval estimates with greater precision than those produced by the conventional inverse variance method. I^2 statistics and the Cochran Q test were used to assess heterogeneity among studies. Subgroup meta-analysis (considering region of the study) and meta-regression (considering year of publication and total sample size) were also performed to investigate the heterogeneity among studies. All statistical tests were two-tailed. Significance was defined as $P < 0.05$. Statistical analyses were performed with R version 3.2.1.

Results

Study selection

The primary literature search identified 811 articles. After title and abstract screening, 20 studies were retrieved for full-text review. Of these, three were excluded because the full-text version could not be retrieved. A fourth study

was excluded for not having a full text version (only a conference abstract had been published). Finally, three additional studies were excluded because data regarding the number or percentage of AITD individuals in each study group (PCOS and controls) was not provided. Therefore, 13 studies were included in the systematic review and meta-analysis (Fig. 1).

Characteristics of the included studies

A summary of the main characteristics of the 13 studies included in the systematic review and meta-analysis is described in Table 1. Seven studies focused on Asian populations: three were performed with Turkish women (32, 33, 34), three with women from India (35, 36, 37) and one with Chinese women (38). Four studies in Europe evaluated German (39), Italian (40), Bulgarian (41) and Slovakian (42) women. Another two studies were performed in Brazilian (43) and Argentinian (44) populations. All studies employed the 2003 Rotterdam criteria for diagnosis of PCOS. AITD diagnosis was based on the criteria defined in each study. Regarding design, there were nine cross-sectional studies (32, 33, 34, 37, 39, 40, 41, 42, 43) and four case–control studies (35, 36, 38, 44)). Population size ranged from 22 to 175 patients, totaling 1210 women with PCOS and 987 healthy controls. In nine studies, age-matched women were selected for inclusion in the comparison group (32, 34, 37, 39, 40, 42, 44), whereas three studies included healthy age-matched and BMI-matched controls (33, 38, 41). In one study, controls were described only as healthy women, without further specification (43). The mean age of PCOS participants ranged from 22 to 30.23 years, vs 20.5 to 33.5 years in comparison groups. Mean BMI ranged from 24.6 to 34.8 kg/m² in PCOS and 21.3 to 29.2 kg/m² in comparison groups (Table 1). NOS score was 9 in six studies (33, 37, 38, 40, 41, 44), 8 in six studies (32, 34, 35, 36, 39, 42) and 7 in one study (43) (Table 2).

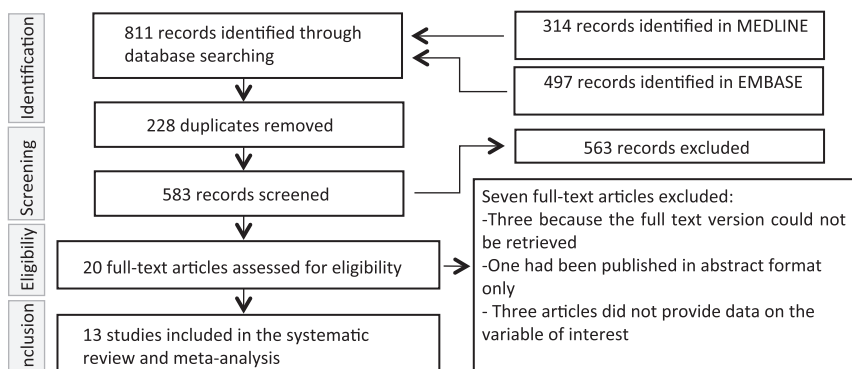


Figure 1 PRISMA flow diagram of the study selection process.

Table 1 Characteristics of studies included in systematic review and meta-analysis investigating the association between polycystic ovary syndrome and autoimmune thyroid disease.

Author, year	Country	Type of study	Comparison group	PCOS				Comparison group				AITD criteria	Main results
				n	Age (mean±s.d.)	BMI (mean±s.d.)	AITD n/%	n	Age (mean±s.d.)	BMI (mean±s.d.)	AITD n/%		
Asia													
Duran et al. 2014 (32)	Turkey	Cross-sectional	Age-matched women without PCOS	73	22 (18–37) ^a	27.45±5.73	23/32.5%	60	20.50 (19–35) ^a	22.55±3.78	14/23.3%	Anti-TPO and/or Anti-Tg positivity and/or heterogeneous thyroid	AITD prevalence was similar between the groups (P<0.05)
Arduc et al. 2015 (33)	Turkey	Cross-sectional	Age and BMI-matched healthy women	86	24.6±6.3	24.9±3.6	19/22.1%	60	26.17±5.0	23.4±2.9	3/5%	Anti-TPO and/or Anti-Tg positivity and hypocholeic thyroid	Higher prevalence of AITD in PCOS group (P<0.0004)
Arora et al. 2015 (35)	India	Case-control	Age-matched women without PCOS	55	23.27±3.2	NA	21/37.72%	51	22.80±4.4	NA	8/15.6%	Anti-TPO and/or Anti-Tg positivity	Higher prevalence of AITD in PCOS group (P<0.05)
Menon et al. 2016 (36)	India	Case-control	Age-matched women without PCOS	90	30.02±8.51	24.6±4.0	23/25%	90	31.4±8.6	21.3±2.8	5/5.6%	Anti-TPO positivity	Higher prevalence of AITD in PCOS group (P<0.05)
Yu et al. 2016 (38)	China	Case-control	Age and BMI-matched healthy women	100	27.4±5.4	31.2±8.3	25/25%	100	23.3±4.1	29.2±5.1	2/2%	Anti-TPO and hypocholeic thyroid	Higher prevalence of AITD in PCOS group (P<0.0001)
Sinha et al. 2017 (37)	India	Cross-sectional	Age-matched women without PCOS	80	22.7±5.30	24.68±3.07	18/22.5%	80	24.3±5.69	23.55±3.02	1/1.25%	Anti-TPO positivity	Higher prevalence of AITD in PCOS group (P<0.05)
Karakose et al. 2017 (34)	Turkey	Cross-sectional	Age-matched healthy women	97	24.1±6.0	27.5±6.0	39/40.2%	71	24.4±4.5	23.4±5.0	11/15.5%	Two of three criteria: Anti-TPO and/or Anti-Tg positivity; hypocholeic thyroid; high levels of TSH	Higher prevalence of AITD in PCOS group (P=0.001)
Europe													
Janssen et al. 2004 (39)	Germany	Cross-sectional	Age-matched women without PCOS	175	28.4±6.5	30.0±7.9	36/20.6%	165	29.8±7.4	25.5±7.1	11/6.5%	Anti-TPO and/or Anti-Tg positivity and hypocholeic thyroid	Higher prevalence of AITD in PCOS group (P=0.001)
Garelli et al. 2013 (40)	Italy	Cross-sectional	Age-matched healthy women	113	24±6.3	NA	30/27%	100	27.1±1.2	NA	8/8%	Two of three criteria: Anti-TPO and/or Anti-Tg positivity; hypocholeic thyroid; high levels of TSH	Higher prevalence of AITD in PCOS group (P<0.0001)

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Author	Country	Study Design	Age and BMI-matched healthy women	n	TSH (mIU/L)	Standard deviation	Median (min-max)	PCOS prevalence	Anti-TPO and Anti-Tg positivity	AITD prevalence	Comparison	
Mitkov et al. 2015 (41)	Bulgaria	Cross-sectional	Age-matched healthy women	70	25.06 ± 0.69	26.50 ± 0.83	14/20%	22	25.78 ± 1.7	23.36 ± 1.4	2/9.09%	AITD prevalence was similar between the groups (P=0.24)
Petrikova et al. 2015 (42)	Slovakia	Cross-sectional	Age-matched healthy women	64	30.23 ± 6.7	28.08 ± 6.91	12/18.75%	68	29 ± 4	21.31 ± 3.05	7/10.29%	Higher prevalence of AITD in PCOS group (P=0.045)
Novais et al. 2014 (43)	Brazil	Cross-sectional	Women without PCOS	65	27.8 ± 6.9	34.8 ± 8.9	28/43.1%	65	33.5 ± 5.7	28.4 ± 4.8	17/26.2%	Higher prevalence of AITD in PCOS group (P=0.04)
Calvar et al. 2015 (44)	Argentina	Case-control	Age-matched healthy women	142	24.5 ± 6.7	29.1 ± 7.9	27/19%	52	26.3 ± 7.4	24.3 ± 4.9	7/13.5%	AITD prevalence was similar between the groups (P < 0.05)

^aMedian (minimum and maximum). AITD, autoimmune thyroid disease; NA, not available; PCOS, polycystic ovary syndrome; S.D., standard deviation; Tg, thyroglobulin; TPO, thyroid peroxidase; TSH, thyroid-stimulating hormone.

Main results

AITD was detected in 315 (26.03%) out of 1210 PCOS women and in 96 (9.72%) out of 987 healthy controls. Geographical stratification revealed the presence of AITD in 28.91, 21.8 and 26.57% of PCOS patients and in 8.59, 7.82 and 20.51% of healthy women from Asia, Europe and South America respectively. Figure 2 shows the individual and pooled odds ratios (ORs) for associations between PCOS and risk of AITD. Overall, a significant association was observed between PCOS and the presence of AITD (OR=3.27, 95% CI 2.32–4.63; P<0.0001). After geographical stratification, the higher chance of AITD in PCOS persisted for Asians (OR=4.56, 95% CI 2.47–8.43), Europeans (OR=3.27, 95% CI 2.07–5.15) and South Americans (OR=1.86, 95% CI 1.05–3.29); however, the difference between subgroups was not statistically significant (P=0.0987).

Between-study heterogeneity was I²=39% (P=0.07). Subgroup analysis by geographic region accounted for 10.81% of this heterogeneity, although statistical significance was not reached (P=0.20). Meta-regression showed that neither year of publication nor total sample size contributed to the observed heterogeneity (<0.1%) (Supplementary Figure 1).

Table 3 describes TSH levels in PCOS and comparison groups. Heterogeneous findings were obtained: six studies demonstrated higher TSH levels in PCOS women compared to the control group (P<0.05) (33, 37, 38, 39, 43, 44). Conversely, five studies did not find a significant difference (P>0.05) (32, 34, 35, 36, 41) between women with PCOS and controls, and one study did not provide TSH data (40). Further analyses were not performed because of the limited amount of data regarding clinical characteristics of PCOS patients with or without AITD in the studies that were selected for analysis.

Discussion

In the present systematic review and meta-analysis, PCOS patients from different populations presented higher likelihood of AITD compared to controls (OR=3.27, 95% CI 2.32–4.63). Of note, higher risk of AITD was detected in Asian populations (OR=4.56, 95% CI 2.47–8.43). However, such differences among the regions were not explained by specific risk factors. Also, there is evidence that thyroid autoimmunity occurs across the world without geographic differences (45). In this sense, the differences in AITD frequency among the studies could be



Table 2 Newcastle–Ottawa Scale for assessing the quality of nonrandomized studies.

Author, year	Score (Stars)			Total score
	Selection	Comparability	Outcome	
Duran <i>et al.</i> 2014 (31)	★★★★	★	★★★	8
Arduc <i>et al.</i> 2015 (32)	★★★★	★★	★★★	9
Arora <i>et al.</i> 2015 (34)	★★★★	★	★★★	8
Menon <i>et al.</i> 2016 (35)	★★★★	★	★★★	8
Yu <i>et al.</i> 2016 (37)	★★★★	★★	★★★	9
Sinha <i>et al.</i> 2017 (36)	★★★★	★★	★★★	9
Karakose <i>et al.</i> 2017 (33)	★★★★	★	★★★	8
Janssen <i>et al.</i> 2004 (38)	★★★★	★	★★★	8
Garelli <i>et al.</i> 2013 (39)	★★★★	★★	★★★	9
Mitkov <i>et al.</i> 2015 (40)	★★★★	★★	★★★	9
Petrikova <i>et al.</i> 2015 (41)	★★★★	★	★★★	8
Novais <i>et al.</i> 2014 (42)	★★★★		★★★	7
Calvar <i>et al.</i> 2015 (43)	★★★★	★★	★★★	9

attributed to variations in AIDT diagnostic criteria and in the size of studied groups.

While thyroid disorders and PCOS are among the most common endocrine conditions in the general

population, the pathophysiological pathway connecting these two disorders has not been clearly established. The mechanism driving the autoimmune attack to the thyroid is complex and includes predominantly

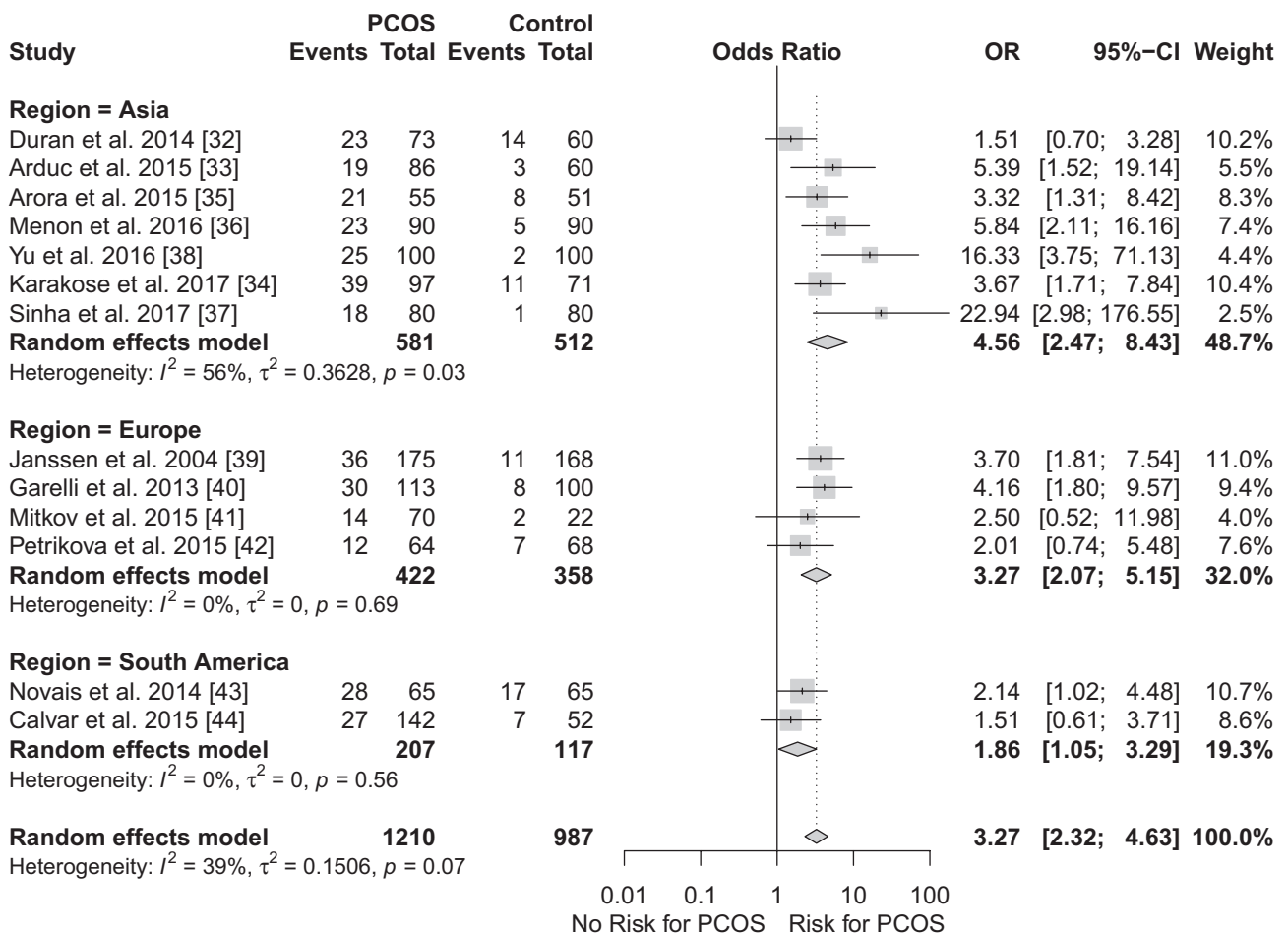


Figure 2 Forest plot showing individual and pooled odds ratios for presence of AITD in women with PCOS in different populations.

genetic, gender-associated and environmental factors such as iodine supply, drugs, infections and chemicals (26, 46). Likewise, the etiology of PCOS is suggested to involve genetic, ovarian-related and other hormonal and metabolic factors such as insulin resistance/compensatory hyperinsulinemia (47). However, a common genetic background has not yet been established.

Abnormal interactions between thyrocytes, antigen-presenting cells and T cells, along with environmental and hormonal factors are found in thyroid disease, producing disturbances in the normal balance between type 1 helper (TH1) and type 2 helper (TH2) lymphocyte immune response. More specifically, TH1-mediated autoimmunity leads to the lysis of thyrocytes and autoimmune hypothyroidism (Hashimoto's thyroiditis), whereas stimulatory TH2 responses against the TSH receptor lead to hyperthyroidism (Grave's disease) (48). PCOS is characterized by androgen excess, which has been shown to be associated with reduction of most

immune system elements, enhancement of T suppressor cell activity, promotion of TH1 response and activation of CD8C (49). In addition, progesterone levels may inhibit macrophage proliferation, IL6 synthesis and peripheral antibody production (50). Also, *in vivo* and *in vitro* data indicate that progesterone has some capacity to suppress CD4+T cell proliferation and TH1 response (51). Indeed, PCOS women often present anovulatory cycles with low luteal phase progesterone levels and higher estrogen-to-progesterone ratio, which may increase their susceptibility to autoimmune disorders. This increased susceptibility may be due, at least in part, to the stimulatory action of estrogens on the immune system (39, 50). In turn, while studies suggest that androgens could provide protection against autoimmune disease, androgen influence on the immune system at the levels observed in PCOS is probably insufficient to prevent autoimmunity (46).

High levels of circulating IFN- γ -inducible protein 10 (IP-10/CXCL10) have been shown in patients with AITD, especially in association with a hypochoic ultrasonographic pattern, which is a sign of a more severe lympho-monocytic infiltration and hypothyroidism (52). In fact, CXCL10 has been suggested as a marker of a stronger and more aggressive inflammatory response in the thyroid, subsequently leading to thyroid destruction and hypothyroidism (26). Interestingly, a recent study has shown that serum CXCL10 concentrations are increased in women with PCOS, which appears to be correlated with the inflammatory and insulin resistance status of PCOS (53).

The most obvious connection between thyroid diseases and PCOS seems to be an increase in BMI and insulin resistance found in both conditions. Increased BMI is very prevalent in women with PCOS, observed in 54–68% of cases (54). Interestingly, although the pathophysiological mechanisms linking thyroid function and obesity have not been clearly established, evidence indicates that TSH is higher in people with high BMI (55, 56). In contrast, recent data have shown that thyroid autoimmunity was not associated with BMI, though a connection with leptin and obesity has been suggested (57, 58). In the present meta-analysis, only 3 out of 13 studies included a BMI-matched control group (33, 38, 41), and higher BMI was found in PCOS compared to controls in most of the studies (32, 34, 36, 39, 42, 43, 44). However, the three studies that stratified PCOS patients with and without AITD did not observe significant differences in BMI, indicating a lack of association between BMI and AITD in PCOS women (39, 40, 44).

Table 3 Studies comparing TSH levels in PCOS and control groups.

Author, year	TSH (mean \pm s.d.)		P value
	PCOS	Comparison group	
Duran <i>et al.</i> 2014 (32)	2.09 (0.67–16.51) ^a	1.96 (0.01–7.08) ^a	0.397
Arduc <i>et al.</i> 2015 (33)	2.9 (0.20–17.9) ^a	1.8 (0.31–5.4) ^a	0.037
Arora <i>et al.</i> 2015 (35)	3.17 \pm 2.74	2.98 \pm 2.18	0.70
Menon <i>et al.</i> 2016 (36)	5.99 \pm 1.8	8.09 \pm 2.4	0.50
Yu <i>et al.</i> 2016 (38)	5.11 \pm 22.7	2.9 \pm 3.2	<0.001
Sinha <i>et al.</i> 2017 (37)	4.547 \pm 2.66	2.67 \pm 3.11	<0.001
Karakose <i>et al.</i> 2017 (34)	2.4 \pm 1.2	2.0 \pm 1.0	0.243
Janssen <i>et al.</i> 2004 (39)	2.0 \pm 1.0	1.4 \pm 0.6	<0.001
Garelli <i>et al.</i> 2013 (40)	NA	NA	NA
Mitkov <i>et al.</i> 2015 (41)	2.46 \pm 0.25	1.73 \pm 0.11	>0.05
Petrikova <i>et al.</i> 2015 (42)	2.37 \pm 1.46	2.37 \pm 1.46	0.937
Novais <i>et al.</i> 2014 (43)	2.9 \pm 1.8	2.2 \pm 1.2	0.013
Calvar <i>et al.</i> 2015 (44)	3.4 \pm 2.8	1.8 \pm 0.9	<0.001

^aMedian (minimum and maximum).

NA, not available; PCOS, polycystic ovary syndrome; s.d., standard deviation; TSH, thyroid-stimulating hormone.



According to large epidemiological surveys, AITD is the most frequent cause of hypothyroidism in the adult population (59, 60, 61, 62). Clinical disease involves a variety of manifestations ranging from simple presence of thyroid antibodies (TAb) in euthyroid patients to severe thyroid dysfunction. Most often, a euthyroid phase is followed by subclinical hypothyroidism (SCH), which slowly progresses to overt hypothyroidism (24). Subclinical hypothyroidism is frequently observed among women with PCOS, with an estimated prevalence range of 10–25% (63). Regarding the impact of subclinical hypothyroidism on the clinical, hormonal or metabolic phenotype of women with PCOS, a recent meta-analysis has shown that the coexistence of SCH and PCOS leads to mild alterations in serum lipids and HOMA-IR, but not in hormone levels (SHBG, FSH, LH and their ratio). These mild changes are not clinically relevant in the short term. The long-term impact of these alterations regarding morbidity has not been established (30). In this sense, further studies searching for the prevalence of PCOS in women with autoimmune thyroid disease could add some additional information regarding the association between these two conditions.

One strength of the present systematic review and meta-analysis is that all studies considered the Rotterdam criteria to diagnose PCOS, ensuring a homogeneous PCOS population. One limitation concerns the fact that AITD diagnosis was assessed according to the authors' chosen criteria. Moreover, because the studies did not provide this information, we were unable to evaluate the differences in TSH levels between PCOS women with or without AITD. The same was true for other clinical characteristics, which were not reported and therefore precluded further comparisons between the two groups. Another limitation is that, despite the absence of significant heterogeneity among studies from different geographical regions, there were limited data from Western European countries and the US. Due to these limitations, the present data should be interpreted with caution.

In conclusion, the present systematic review and meta-analysis provides evidence of higher prevalence of AITD in patients with PCOS compared to healthy controls. Therefore, physicians should consider screening for thyroid function and thyroid-specific autoantibodies at PCOS diagnosis, even in the absence of symptoms related with thyroid dysfunction.

Supplementary data

This is linked to the online version of the paper at <https://doi.org/10.1530/EC-18-0309>.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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