



Endometriosis, autoimmunity and ovarian reserve: a research note


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Abstract

Objectives: to assess ovarian reserve in women with endometriosis according to the presence of antithyroid antibodies.

Methods: retrospective cross-sectional study conducted in assisted reproduction clinics in Recife, Brazil, from February 2017 to August 2021. Women aged 18–49 years with endometriosis and recorded measurements of anti-TPO and/or anti-Tg, anti-Müllerian hormone (AMH), and antral follicle count (AFC) were included. Women with other causes of diminished ovarian reserve were excluded. Numerical variables were compared using the Mann–Whitney test, with $p < 0.05$ considered significant.

Results: of 83 eligible women, 48 were analyzed: 14 (29.2%) antibody-positive and 34 (70.8%) negative. Age and body mass index were similar between groups. No significant differences were found in TSH or free T4 levels. Median AMH was 0.66 ng/mL in the positive group and 1.37 ng/mL in the negative group ($p = 0.09$), and AFC was 7.5 vs. 10.0, respectively ($p = 0.41$).

Conclusions: among women with endometriosis, a high prevalence of thyroid autoantibodies was observed. There were no statistically significant differences in ovarian reserve markers between groups, although a trend toward lower AMH values was seen among antibody-positive participants. Future studies with larger samples may confirm or modify these findings.

Key words Hashimoto disease, Autoimmune thyroiditis, Ovarian reserve, Fertility, Endometriosis, Autoimmunity



Introduction

Endometriosis is a chronic, estrogen-dependent inflammatory disease that affects approximately 10% of women of childbearing age, and is associated with infertility, pelvic pain and impaired quality of life.^{1,2} In addition to local mechanisms, there is increasing evidence that systemic immunological and inflammatory alterations participate in the disease's pathophysiology.^{3,4}

Highlighted among these alterations is the potential relationship between endometriosis and autoimmune disorders, particularly those of the thyroid.^{5,6} The presence of anti-thyroid antibodies [anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg)] is common in women with endometriosis, potentially representing a subclinical autoimmune condition that affects ovarian functions.^{7,8} However, the literature reveals conflicting results regarding the impact of thyroid autoimmunity on ovarian reserve, which is estimated by markers such as the Anti-Müllerian Hormone (AMH), and the Antral Follicle Count (AFC).^{9,10}

Given these uncertainties, this study aimed to evaluate the ovarian reserve of women with endometriosis, based on the positivity of anti-thyroid antibodies.

Methods

This was a retrospective cross-sectional study conducted at assisted reproduction clinics in the f Recife, Pernambuco, Brazil, between February 2017 and August 2021. Women aged 18 to 49 years with endometriosis diagnosis, confirmed by ultrasound or laparoscopy, and laboratory records of AMH, AFC and anti-TPO and/or anti-Tg were included.

Participants with a history of ovarian surgery, chemotherapy, pelvic radiotherapy, recent utilization of hormonal contraceptives, early menopause or acknowledged endocrine diseases that could interfere with ovarian reserve were excluded. Clinical variables included age, body mass index (BMI), serum levels of thyroid-stimulating hormone (TSH) and free thyroxine (FT4).

The AMH and AFC values were compared between the groups with or without antibody positivity. Statistical analysis was conducted using SPSS software, version 20.0, employing Mann-Whitney test for numeric variables and the chi-square test for categorical variables, with $p < 0.05$ considered statistically significant.

The study was approved by the Research and Ethics Committee of the institution, under CAAE N°. 66226122.5.0000.5201 and opinion N°. 5.971.732, on March 29, 2023.

Results

Of the 83 women initially eligible, 48 met the inclusion criteria, as described in the selection flowchart (Figure 1). Of these, 14 (29.2%) tested positive for antithyroid antibodies and 34 (70.8%) tested negative.

The general clinical and hormonal characteristics are presented in Table 1. The mean ages were 34.7 ± 5.8 and 35.2 ± 6.1 years, respectively, with no significant difference between the groups ($p = 0.72$). Body Mass Index (BMI) was also similar (23.4 ± 2.7 vs. 23.1 ± 3.0 kg/m²; $p = 0.68$).

No significant differences were observed in serum TSH levels (2.1 ± 0.7 vs. 2.3 ± 0.9 μ IU/mL; $p = 0.54$) and FT4 (1.1 ± 0.2 vs. 1.2 ± 0.3 ng/dL; $p = 0.41$). Ovarian reserve markers showed median AMH levels of 0.66 ng/mL in the autoantibody-positive group and 1.37 ng/mL in the negative group ($p = 0.09$). The median AFC levels of 7.5 and 10.0, respectively ($p = 0.41$), as shown in Table 2.

A trend towards lower AMH values was observed among women with thyroid autoimmunity, although it did not reach statistical significance. No relevant correlation was found between TSH and AMH levels ($r = -0.11$; $p = 0.39$).

Discussion

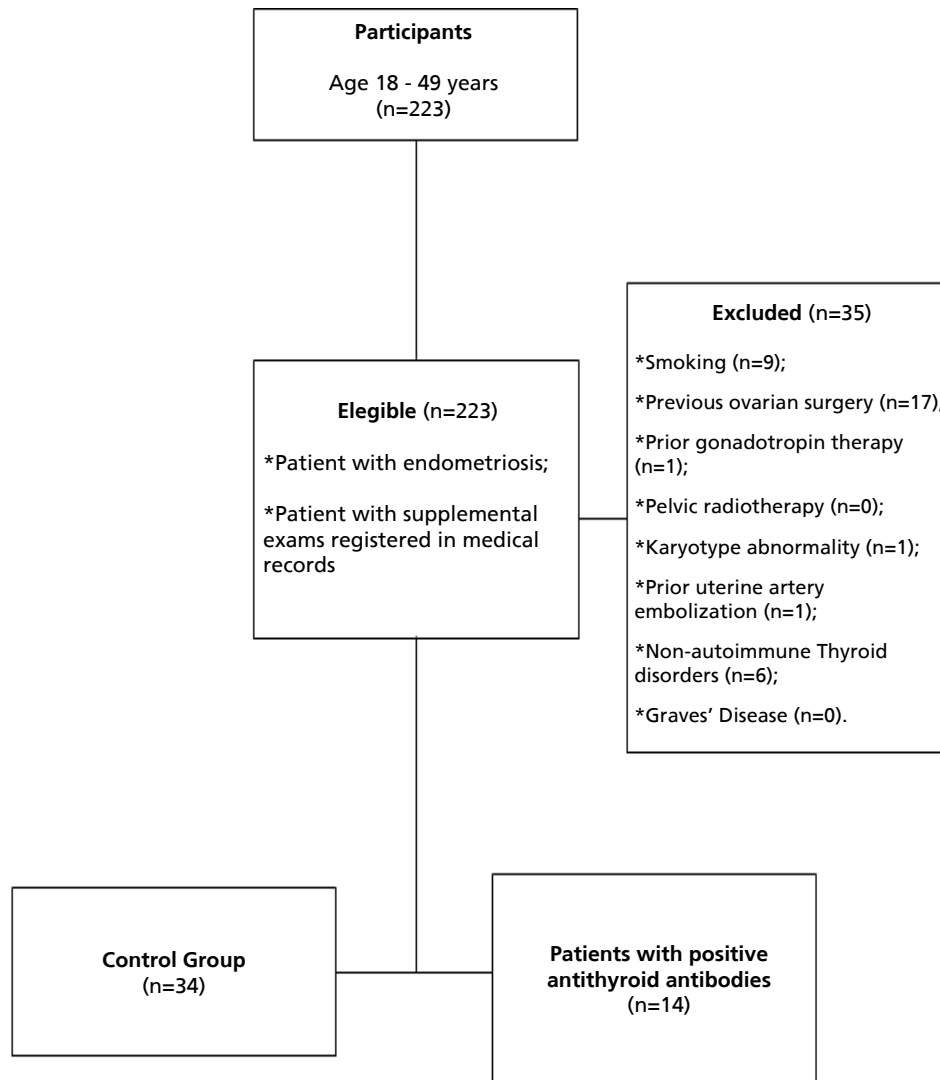
The association between endometriosis and autoimmune disorders, particularly thyroid disorders, has been reported by different studies, suggesting that systemic inflammatory processes and immune alterations may be involved with both conditions.¹⁻⁴ The presence of anti-thyroid antibodies, such as anti-TPO and anti-Tg, reflects autoimmune activity that may interfere with steroidogenesis and folliculogenesis, thereby indirectly affecting the ovarian reserve.^{5,6}

In this sample of women with endometriosis, the prevalence of thyroid autoimmunity was high (29.2%); however, no significant differences in AMH and AFC were observed between the positive and negative groups. These findings are consistent with those reported by Osuka *et al.*⁷ and Notaro *et al.*,⁸ who also found no statistically significant association between thyroid antibodies and diminished ovarian reserve.

Studies with larger samples, however, indicate that subtly lower AMH levels may occur in women with antibody positivity, suggesting a potential follicular damage mediated by inflammation or cytokine-induced apoptosis.⁹⁻¹¹ Such differences may depend on the stage of the disease, reproductive age and laboratory criteria utilized to define positivity.

Figure 1

Flowchart of the selection of participants included in the study.



Note: clear description of the screening process, exclusions by criteria, and final sample (n=48).

Table 1

Clinical and hormonal characteristics of women with endometriosis, according to the presence of antithyroid antibodies. Recife, Pernambuco, 2017/2021.

Variable	Anticorpos antitireoidianos		PR (95%CI)	p
	Positive (N=14)	Negative (N=34)		
Age, years (Med; IQR)	37.5; 36.0 - 40.0	37.0; 35.0 - 39.0	-	0.51*
BMI, kg/m ² (Med; IQR)	25.4; 22.90 - 27.81	24.61; 21.80 - 26.70	-	0.34*
Infertility (n; %)				
Yes	11; 78.57	29; 85.29	0.92 (0.68 - 1.25)	0.67**
No	3; 21.43	5; 14.71		
Autoimmune diseases (n; %)				
Yes	0; 0	2; 5.88	-	1.00**
No	14; 100.0	32; 94.12		
Overt hypothyroidism (n; %)				
Yes	2; 14.29	1; 2.94	4.86 (0.48-49.35)	0.20**
No	12; 85.71	33; 97.06		

*Mann-Whitney Test; ** Fisher's Exact Test; BMI= body mass index; Med= Median; IQR= interquartile range; PR= Prevalence Ratio; CI= Confidence Interval.

Table 2

Ovarian reserve markers according to the presence of antithyroid antibodies. Recife, Pernambuco, 2017/2021.

Variable	Antithyroid antibodies		PR (95%CI)	p
	Positive (N=14)	Negative (N=34)		
TSH mIU/L (Med; IQR)	2.03; 1.0 - 2.86	2.09; 1.5 - 2.5	-	0.52*
FT4 ng/dL (Med; IQR)	1.18; 1.0 - 1.22	1.13; 1.04 - 1.29	-	0.75*
AMH ng/ml (Med; IQR)	0.66; 0.39 - 1.49	1.37; 0.7 - 2.5	-	0.09*
AFC (Med; IQR)	7.5; 4 - 11	10; 5 - 19	-	0.41*
Anti-TPO IU/ml (n; %)	11; 78.57	-	-	-
Anti-Tg IU/ml (n; %)	6; 42.86	-	-	-

Med= Median; IQR= Interquartile Range; TSH= thyroid-stimulating hormone; T4= thyroxine; AMH= Anti-Müllerian Hormone; AFC= Antral Follicle Count; Anti-TPO= anti-thyroid peroxidase antibodies; Anti Tg= Anti-thyroglobulin antibodies; PR=Prevalence ratio; CI= Confidence interval; *Mann-Whitney test.

The main limitations of this study include the retrospective design, the small sample size, and the lack of control for potential confounders, such as the duration of endometriosis and prior use of hormone therapy. Nevertheless, the consistency of findings with the literature reinforces the notion that isolated thyroid autoimmunity may not exert a clinically relevant impact on the ovarian reserve in women with endometriosis.¹²⁻¹⁴

The coexistence of endometriosis and thyroid autoimmunity reinforces the complexity of the interface among inflammation, immunity and female fertility. Although no statistically significant difference was observed in the ovarian reserve makers, the trend towards lower AMH levels in seropositive women suggests a potential subclinical influence of autoimmunity over ovarian function. Prospective studies, with greater statistical power and standardization of diagnostic and laboratory criteria will be essential to clarify the role of thyroid autoimmunity on reproductive pathophysiology and the clinical management of endometriosis.

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Authors' contribution

Souza ASR and Notaro LGR: conceptualization and study design, data collection and analysis, manuscript writing and review. Ferreira MER, Gomes RC, Rios SV, Chacon VO and Viana MAB: data collection and interpretation and drafting and critical review of the manuscript. All authors approved the final version of the article and declared no conflicts of interest.

Data Availability

All datasets supporting the study are included in the article.

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