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Is Every Thyroid Antibody a Bad Sign?: The Complex Relationship of Antithyroid Antibodies and Obsessive-compulsive Symptoms

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Objective: Several immunological factors are emphasized in the etiology of autoimmune thyroid diseases and obsessive-compulsive disorder. Obsessive-compulsive symptoms (OCS) are commonly seen in patients with autoimmune thyroid diseases. This study aims to evaluate the relationship between OCS and antithyroid antibodies.
Methods: The study included 145 patients with Hashimoto thyroiditis or Graves' disease and 42 healthy controls. Thyroid function tests and serum thyroid autobody levels (anti-thyroglobulin [TG], anti-thyroid peroxidase [TPO], and anti-thyroid stimulating hormone [TSH]) of the patients were measured. The socio-demographic data and OCS of the participants were evaluated with Dimensional OCS (DOCS).
Results: DOCS scores were higher in patients than in the control group. There was not found a significant relationship between free T3, free T4, and TSH levels and DOCS scores. Anti-TG positivity in females was associated with lower DOCS scores. Anti-TPO positivity in males had a positive correlation with DOCS scores. There was no correlation between sex and the presence of anti-TSH in terms of OCS severity. Univariate analysis found the highest OCS scores in anti-TPO positive, anti-TG, and anti-TSH negative patients. The group with the lowest OCS scores was found to be anti-TG positive, anti-TPO, and anti-TSH negative patients.
Conclusion: OCS severity could be affected by different thyroid autoantibody profiles in patients with autoimmune thyroid diseases. While anti-TG serves a protective role against OCS in females, the presence of anti-TPO may worsen the OCS in men. Additionally, the co-existence of different antithyroid antibodies may affect the severity of OCS differently according to sex.

KEY WORDS: Obsessive-compulsive disorder; Hashimoto disease; Graves disease; Autoimmunity; Autoantibodies.

INTRODUCTION

Hashimoto's disease, which is considered among the important and common diseases of the thyroid, is an inflammation caused by autoantibodies against the thyroid gland. It is a slowly progressive disorder thatusually presents with hypothyroidism clinically. Its prevalence is about 0.3−1.5% and it is observed 10−15 times more frequently in females [1]. Another important disease of the thyroid gland is Graves' disease, which is also the most frequently observed autoimmune disease inthe general population. Graves' disease is mainly observed in females between 40−60 years old and mostly presents with symptoms of hyperthyroidism [2]. It occurs due to autoantibodies developing against thyroid stimulating hormone receptors (anti-TSH) on the surface of thyroid follicular cells. It can be triggered by factors such as stressful life events, infections, and birth based on genetic predisposition [3]. In both diseases, physical symptoms are also frequently accompanied by neuropsychiatric symptoms. These neuropsychiatric symptoms are thought to be caused by changes in thyroid hormone levels as well as

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other etiological factors that play a role in the pathophysiology of the diseases [4].

The role of autoantibodies against thyroid tissue is important in the etiology of both diseases. However, these autoantibodies can also cause a reaction against brain tissue. One of the most important clinical examples of this situation is a severe neuropsychiatric picture called Hashimoto's encephalopathy accompanied by EEG abnormalities and other neurological symptoms and responding rapidly to steroid treatments [5]. Milder or different variants of this picture may present with different psychiatric manifestations. For example, in a study investigating the frequency of thyroid autoantibodies (anti-thyroglobulin (anti-TG) and anti-microsomal antibodies) in the psychiatric patient population, the presence of these antithyroid antibodies was reported at a rate of 9% in affective disorders and 10% in other psychiatric disorders [6].

Obsessive-compulsive disorder (OCD) is one of the psychiatric diseases that deteriorates the quality of life and causes disability. OCD consists of thoughts, impulses, or images (obsessions) that intrusively come to mind and stimulate a subjective feeling of discomfort, and actions such as counting, washing, and checking (compulsions) that are required to reduce or neutralize their effects [7]. Although its etiology points to complex biopsychosocial pathophysiology, interest in the biological etiology of the disorder has increased in recent years. While functional studies such as brain imaging, positron emission tomography, and single-photon emission computerized tomography target the basal ganglia [8], the autoimmune and inflammatory processes are also frequently emphasized in its etiology [9].

It has been reported that OCD is more common in patients with autoimmune thyroid diseases than in healthy controls [10]. Although the relationship between autoimmune thyroid diseases and OCD has been shown, there are onlya few studies concerning associations between antithyroid antibodies and obsessive-compulsive symptoms (OCS) or OCD [11]. In a study comparing patients diagnosed with OCD and depressive disorder, no difference was found between the groups in terms of thyroid peroxidase antibody (anti-TPO) and anti-TG levels [12]. Only one study with a limited number of participants showed a positive association between anti-TPO levels and OCD subscales in the Symptom Check List-90 scale (SCL-90) [13].

This study aims to investigate whether there is a relationship between autoimmune thyroid diseases and OCS and if there is, what kind of relationship there is between OCS and antithyroid antibodies.

METHODS

Participants and Procedure

A total of 187 participants, 145 patients and 42 healthy volunteers, aged 18－65 years, who gave written consent to participate in the study, were included. The patient group consisted of patients diagnosed with Hashimoto's thyroiditis or Graves' disease as a result of the examinations performed in the endocrinology department. Diagnosis is based on clinical features of patients (dysphonia, dysphagia, dyspnea, constipation, dry, cold, and pale skin, bradycardia, loss of concentration, memory problems, depression), presence of serum autoantibodies against thyroid antigens (anti-TPO, anti-TG, anti-TSH) or thyroid ultrasonography (USG). Radioactive iodine reuptake and thyroid aspiration cytology were rarely used. Patients with chronic uncontrolled medical illness were excluded from the study.

The patients were evaluated with a semi-structured interview by the psychiatrist. Patients with any psychiatric diagnosis (including psychotic disorder, depression, anxiety disorder, and OCD) or using illicit substance or psychotropic drugs were not included in the study. The healthy control group was selected from participants who did not have any chronic medical or psychiatric diseases, were not on any regular medication, and did not have any medical or psychiatric complaints lasting more than two weeks in the last 6 months.

Serum anti-TG, anti-TPO, and anti-TSH levels, sedimentation rate, and C-reactive protein (CRP) values, free T3 (fT3, reference: 2.3－4.2 ng/dl), free T4 (fT4, reference: 0.89－1.76 ng/dl) and TSH (reference: 0.55－4.78 mU/L) values, thyroid USG records belonging to the participants in the patient group and requested by the endocrinology department for diagnostic purposes were examined. These endocrinological and immunological parameters were not examined in the control group. Values $\geq$ 4.5 IU/ml for anti-TG antibodies, $>$ 60 U/ml for anti-TPO, and $\geq$ 1.75 IU/L for anti-TSH were considered cut-off values.

Dimensional OCS (DOCS) was administered to each participant. This scale is developed by Abramowitz *et al.*

[14] and contains four distinct obsessive-compulsive symptom dimensions (contamination,responsibility for harm or mistakes, unacceptable thoughts, and incompleteness), each of which contains general definitions and examples. DOCS measures the severity of each symptom dimension, including avoidance behavior. It consists of four dimensions with five items scored between 0−4 and Turkish validity and reliability study of the scale was performed [15].

The study protocol was reviewed and approved by Yildirim Beyazit University Institutional Ethics Committee (date 17.03.2021, approval number: 24). Our study was performed in accordance with the Declaration of Helsinki regarding the ethical principles for medical research involving human subjects. Written informed consent was obtained from all participants.

Statistical Analysis

Continuous variables were shown as mean and standard deviation and discrete variables as frequency and percentage. In paired comparisons, Student *t* test was used for continuous variables and the chi-square test was used for discrete variables. Correlations between thyroid autoantibodies and obsessive-compulsive symptomatology were analyzed by Pearson correlation analysis.

Relationship between thyroid autoantibodies, gender, and OCS; main effects for sex, anti-TG, anti-TPO, anti-TSH, fT3, fT4, TSH variables and sex*anti-TG, sex*anti-TPO, sex*anti-TSH, sex*anti-TG*anti-TPO and antiTG* antiTPO were tested with the univariate model for interaction effects. The statistically significant cut-off value was accepted as $p < 0.05$.

RESULTS

The study included 145 patients and 42 healthy controls. The mean age of the patient group was 29.86 ± 10.94 years and the control group was 45.36 ± 14.00 years. There was a significant difference in ages between the groups ($t = -6.609$, $p < 0.001$). There were 113 (78.5%) females in the patient group and 31 (73.8%) females in the control group. There was no significant difference between the groups in terms of sex ($\chi^2 = 0.404$, $p = 0.525$).

Hashimoto's thyroiditis was diagnosed in 85 (58.6%) patients and Graves' disease was diagnosed in 60 (41.4%) patients. 114 (78.6%) patients were followed up with medication (levothyroxine or propylthiouracil), and 26 (17.9%) people were followed without any medication. In 5 (3.6%) patients, both drug and surgical treatment were recommended. fT4 values were normal in 115 (79,3%), low in 8 (5.5%), and high in 20 (13.8%) of patients. fT3 values normal in 121 (83.4%), low in 8 (5.5%), and high in 11 (7.4%) of patients. TSH levels were normal in 55 (37.9%) of the patients, low in 33 (22.8%), and high in 54 (37.2%). Anti-TPO was positive in 95 (65.5%) of patients, anti-TG was positive in 67 (50.4%), and anti-TSH was positive in 32 (22.1%) of patients.

There was a significant difference between the DOCS total and subscalescores between the patient and control groups. All subscales and total scores of the patient group were higher than the control group (Table 1). When Hashimoto and Graves' patient groups were compared, no significant difference was found between the groups in terms of DOCS total and subscale scores ($p > 0.05$).

Table 1. Comparison of DOCS total and subscale scores between the patient group and healthy controls

DOCS subgroups	Group	Mean ± SE	95% CI	
			Lower bound	Upper bound
Total (F = 20.373, $p < 0.001$)	Control	5.06 ± 2.11	0.88	9.24
	Patient	18.85 ± 1.09	16.68	21.01
Contamination (F = 20.219, $p < 0.001$)	Control	1.80 ± 0.62	0.56	3.04
	Patient	5.10 ± 0.32	4.45	5.74
Responsibility for harm or mistakes (F = 25.293, $p < 0.001$)	Control	0.98 ± 0.61	−0.22	2.20
	Patient	4.59 ± 0.31	3.96	5.22
Unacceptable thoughts (F = 23.488, $p < 0.001$)	Control	1.17 ± 0.64	−0.10	2.45
	Patient	4.84 ± 0.33	4.17	5.50
Incompleteness (F = 20.015, $p < 0.001$)	Control	1.09 ± 0.61	−0.11	2.31
	Patient	4.31 ± 0.31	3.68	4.94

Covariates appearing in the model are evaluated at the following values: age = 41.73.
DOCS, Dimensional Obsessive-Compulsive Scale; SE, standard error; CI, confidence interval.

When the relationship between thyroid hormones and DOCS total and subscales was examined with the univariate model, no significant relationship was found between fT3, fT4, and TSH levels and DOCS total and subscales scores ($p > 0.05$). Furthermore, no significant correlation was found between sedimentation and CRP and OCS ($p > 0.05$). According to the correlation analysis between antithyroid antibodies and DOCS total and subscales scores, a weak, inverse but significant correlation was found between anti-TG positivity and DOCS total and subscales scores. No significant correlation was found between DOCS total and subscores and fT3 and TSH levels, but a weak and inversely significant correlation was found between fT4 and DOCS responsibility for harm or mistakes, unacceptable thoughts, and incompleteness sub-scale and total scores (Table 2).

When the relationship between sex and anti-TG was examined in the post hoc analyzes of univariate 2 × 2 comparisons, the severity of OCS was significantly higher in anti-TG negative females than in anti-TG positive females ($p = 0.005$). There was no significant effect of anti-TG levels on OCS severity in the male sex ($p > 0.05$). When the interaction between sex and anti-TPO was examined, the OCS score was significantly higher in males with anti-TPO positivity than in males with negative anti-TPO ($p = 0.008$). Similarly, OCS was statistically significantly higher in males with positive anti-TPO compared to females with positive or negative anti-TPO ($p = 0.025$, $p = 0.013$). When the interaction between sex and anti-TSH was examined, no statistically significant difference was found between the groups in terms of OCS severity ($p > 0.05$) (Table 3).

In post hoc analyses examining the interaction of anti-TPO and anti-TG antibodies, DOCS scores were statistically significantly higher in patients with anti-TG negative and anti-TPO positive compared to the patients with anti-TG positive and anti-TPO either positive or negative ($p = 0.04$, $p = 0.018$) (Table 3).

2 × 2 × 2 univariate analyzes for each group are shown in Table 4. When the relationship between sex, anti-TG, and anti-TPO was examined, male patients with anti-TG negative and anti-TPO positive had the highest DOCS scores. The lowest OCS score was in anti-TG positive and anti-TPO negative male patients.

According to the comparisons in which the relationship between sex, anti-TG, and anti-TSH was examined, the highest total DOCS score was found in female patients with anti-TG and anti-TSH negative. The group with the lowest total DOCS score were female patients who were positive for anti-TG and anti-TSH (Table 4).

When the relationship of anti-TG, anti-TPO, and anti-TSH antibodies was examined by a 2 × 2 × 2 univariate comparison, the patients with the highest OCS score were anti-TPO positive, anti-TG and anti-TSH negative. The group with the lowest OCS scores was found to be anti-TG positive, anti-TPO and anti-TSH negative patients (Table 4).

Table 2. Correlation between thyroid auto antibodies and DOCS total and subscale scores

DOCS subscores	Anti-TG	Anti-TPO	Anti-TSH	Free T3	Free T4	TSH
Total						
r	−0.271*	0.032	−0.073	−0.105	−0.206*	0.075
p	0.002*	0.708	0.443	0.225	0.016*	0.382
Contamination						
r	−0.261*	−0.052	−0.042	−0.050	−0.135	0.093
p	0.003*	0.546	0.655	0.563	0.113	0.281
Responsibility for harm or mistakes						
r	−0.247*	−0.012	−0.099	0.008	−0.212*	0.085
p	0.005*	0.887	0.293	0.930	0.012*	0.321
Unacceptable thoughts						
r	−0.183*	0.094	−0.109	−0.126	−0.244*	0.178
p	0.038*	0.271	0.250	0.144	0.004*	0.038
Incompleteness						
r	−0.199*	0.043	−0.060	−0.073	−0.205*	0.136
p	0.024*	0.619	0.526	0.400	0.016*	0.112

Anti-TG, anti thyroglobulin antibody; Anti-TPO, anti thyroid peroxidase antibody; Anti-TSH, anti thyroid stimulating hormone antibody; DOCS, Dimensional Obsessive-Compulsive Scale.
*$p < 0.05$.

Table 3. Univariate 2 × 2 analysis results showing the relationship between thyroid auto anti bodies and DOCS total scores

Factor 1	Factor 2	DOCS score (mean ± SE)	95% CI	
			Lower	Upper
Female	Anti-TG negative	21.08* ± 2.35	16.46	25.69
	Anti-TG positive	12.07* ± 2.13	7.88	16.26
Male	Anti-TG negative	20.75 ± 4.13	12.63	28.86
	Anti-TG positive	12.04 ± 5.06	2.10	21.97
Female	Anti-TPO negative	16.74* ± 2.52	11.80	21.68
	Anti-TPO positive	16.41* ± 1.94	12.60	20.21
Male	Anti-TPO negative	11.25* ± 4.55	2.32	20.17
	Anti-TPO positive	26.68* ± 3.65	19.52	33.84
Female	Anti-TSH negative	19.50 ± 1.67	16.21	22.79
	Anti-TSH positive	13.65 ± 2.70	8.35	18.94
Male	Anti-TSH negative	15.34 ± 3.27	8.91	21.76
	Anti-TSH positive	18.50 ± 7.30	4.18	32.81
Anti-TG negative	Anti-TPO negative	18.60 ± 3.20	12.32	24.88
	Anti-TPO positive	24.04* ± 2.95	18.25	29.84
Anti-TG positive	Anti-TPO negative	9.38* ± 4.10	1.34	17.42
	Anti-TPO positive	15.62* ± 1.97	11.75	19.49

DOCS, Dimensional Obsessive-Compulsive Scale; Anti-TG, anti thyroglobulin antibody; Anti-TPO, anti thyroid peroxidase antibody; Anti-TSH, anti thyroid stimulating hormone antibody; SE, standard error; CI, confidence interval.
*$p < 0.05$.

Table 4. 2 × 2 × 2 univariate analysis results on the relationship between thyroid auto antibodies and DOCS total scores

Factor 1	Factor 2	Factor 3	DOCS scores (mean ± SE)	95% CI	
				Lower	Upper
Female	Anti-TG negative	Anti-TPO negative*	22.71 ± 3.65	15.46	29.96
		Anti-TPO positive*	19.92 ± 3.52	12.92	26.93
	Anti-TG positive	Anti-TPO negative*	10.76 ± 4.03	2.75	18.78
		Anti-TPO positive*	13.37 ± 2.24	8.92	17.83
Male	Anti-TG negative	Anti-TPO negative	14.50 ± 5.88	2.82	26.17
		Anti-TPO positive*	33.25 ± 6.44	20.46	46.04
	Anti-TG positive	Anti-TPO negative*	8.00 ± 7.88	−7.66	23.66
		Anti-TPO positive	20.12 ± 4.55	11.08	29.16
Female	Anti-TG negative	Anti-TSH negative	25.88* ± 2.24	21.43	30.34
		Anti-TSH positive	16.75 ± 4.55	7.70	25.79
	Anti-TG positive	Anti-TSH negative	13.59* ± 2.82	7.97	19.21
		Anti-TSH positive	10.55* ± 3.65	3.30	17.80
Male	Anti-TG negative	Anti-TSH negative	19.62 ± 4.91	9.85	29.39
		Anti-TSH positive	23.00 ± 9.10	4.91	41.08
	Anti-TG positive	Anti-TSH negative	11.06* ± 5.09	0.95	21.17
		Anti-TSH positive	14.00 ± 12.88	−11.58	39.58
Anti-TG negative	Anti-TPO negative	Anti-TSH negative	15.96* ± 4.09	7.82	24.10
		Anti-TSH positive	21.25 ± 5.57	10.17	32.32
	Anti-TPO positive	Anti-TSH negative	29.55* ± 3.52	22.54	36.55
		Anti-TSH positive	14.00* ± 6.44	1.21	26.79
Anti-TG positive	Anti-TPO negative	Anti-TSH negative	7.64* ± 5.16	−2.61	17.89
		Anti-TSH positive	11.12* ± 7.20	−3.17	25.42
	Anti-TPO positive	Anti-TSH negative	17.01* ± 2.69	11.66	22.36
		Anti-TSH positive	12.85* ± 3.44	6.02	19.69

DOCS, Dimensional Obsessive-Compulsive Scale; Anti-TG, anti thyroglobulin antibody; Anti-TPO, anti thyroid peroxidase antibody; Anti-TSH, anti thyroid stimulating hormone antibody; SE, standard error; CI, confidence interval.
*$p < 0.05$.

DISCUSSION

To the best of our knowledge, this is the first study to investigate the associationbetween circulating thyroid autoantibodies and OCS severity in patients with autoimmune thyroid disorders. This study revealed that OCS severity are higher in patients with autoimmune thyroid disorders than the healthy controls. Additionally, it has been shown that there is a correlation between the severity of OCS and thyroid autoantibodies. While anti-TG positivity in the female gender decreases OCS severity, anti-TPO positivity in males has a positive correlation with OCS severity. Moreover, the co-existence of thyroid autoantibodies in different combinations may affect the severity of OCS differently.

The possible mechanisms of autoimmune thyroid diseases on the pathophysiology of psychiatric disorders are inconclusive. As the systemic inflammation seen in autoimmune disorders may affect the central nervous system (CNS), anti-thyroid antibodies may also have direct effects on the CNS [16]. It has been shown that antithyroid antibodies have targets localized at the specific sites of the CNS. The anti-TSH receptor antibodies have antigenic targets on cortical neurons and anti-TG antibodies in the cerebral vasculature [17]. It is speculated that antithyroid antibodies might increase autoimmune susceptibility in the CNS by causing vasculitis and dysfunction in the blood-cerebrospinal fluid (CSF) barrier [18]. Anti-thyroid antibodies are believed to disturb blood-CSF barrier, thus lead an interaction between peripheral immunity and CNS which may induce central autoimmune mechanisms and cause neuronal damage [18]. However, in these possible pathophysiological mechanism explanations, the specific roles of each autoantibody have not been clearly elucidated.

Although the relationship between thyroid autoantibodies and OCS has not been studied, there are studies on the relationship of thyroid autoantibodies with symptom severity and treatment response in affective disorders. In patients with thyroid autoantibodies, the symptom severity of depression was reported higher than the patients with negative antibodies [19]. The thyroid autoantibody positivity was also associated with poor response to antidepressant therapy in depressive patients [20]. In a study conducted with bipolar disorder patients, the presence of anti-TPO was found to be related to rapid-cycling [21], while another study did not reveal differences in the prevalence of thyroid antibodies in rapid-cycling bipolar patients [22].

Even though the majority of findings suggest that antithyroid antibodies affect the clinical course negatively in psychiatric diseases such as affective disorder, our study showed that each thyroid autoantibody and their combinations have different effects on the severity of OCS in different sex. Anti-TPO levels were significantly associated with higher OCS scores only in the male patients. Contrary to expectations, anti-TG antibodies were found to be negatively correlated with OCS severity, especially in the female sex.

It is known that there is a greater prevalence of autoimmune disease in females than males in general and their clinical course may also vary between sex. Sex hormones, differences in reproductivity, and extrinsic epigenetic factors are thought to have roles in increased autoimmunity in females [23]. Regarding thyroid antibodies, middle-aged females are known to show higher positivity [24]. These differences in antibody profiles and autoimmunity can be thought to change the prognostic effects of antibodies in OCS between sex.

When the literature is examined, it is seen that autoimmune diseases have heterogeneous clinical manifestations and some autoimmune markers have different prognostic effects on the clinical course. As an example, when the clinical course of systemic lupus erythematosus is examined, it has been proven that some IgM antibodies serve as a natural immune repertoire that provides homeostatic functions and prevents certain organ damage by playing a protective role [25]. Similarly, it is observed that older females with anti-TPO antibodies experience a better general health condition than females without anti-TPO. Additionally, the presence of anti-TPO antibodies has been shown a positive prognostic effect in patients with breast cancer [26].

It is proposed that differences in the location of antibody receptors, antibody levels in the serum, duration of antibody exposure, and immunological mechanisms may cause antibodies to act differently [27]. The definition of the 'autoimmune OCD' subtype has recently been proposed [9], and the different clinical effects of these antibodies on OCS symptoms could be important when identifying the autoimmune basis of OCD. In the light of these examples, it could be speculated that each antithyroid an-

tibody may have specific effects on the different parts of the brain, and various combinations of these antibodies may alter neuronal inflammation and immunity in different ways.

Our findings must be considered in the view of some limitations. The main limitation is that it is a cross-sectional study and the antibodies were measured only once. The study was conducted with a relatively small number of participants for assessing antithyroid antibodies. Although some antibodies such as anti-TG may be frequently positive in the general population, the antithyroid antibody levels of the control group could not be measured. As antithyroid antibodies are very prevalent in the population, the concomitant occurrence of OCS and antibody positivity may be due to chance. On the other hand, this study has the advantageof being the first study that evaluates the serum levels ofthe most important thyroid antibodies and their correlation with OCS severity comprehensively.

In conclusion, there is a clear relationship between thyroid autoimmunity and OCS. Symptom severity could be affected by different thyroid autoantibody profiles and certain antithyroid antibodies serve a protective role against OCS severity according to gender. The mechanism of how each thyroid autoantibody has a specific effect on the braincould be the subject of further research.

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■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

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REFERENCES

1. Lorini R, Gastaldi R, Traggiai C, Perucchin PP. *Hashimoto's thyroiditis. Pediatr Endocrinol Rev 2003;1 Suppl 2:205-211; discussion 211.*
2. Brent GA. *Clinical practice. Graves' disease. N Engl J Med 2008;358:2594-2605.*
3. Manji N, Carr-Smith JD, Boelaert K, Allahabadia A, Armitage M, Chatterjee VK, *et al. Influences of age, gender, smoking, and family history on autoimmune thyroid disease phenotype. J Clin Endocrinol Metab 2006;91:4873-4880.*
4. Sobolevskaia PA, Andreev BV, Gvozdetckii AN, Dolina AA, Stepochkina AM, Stroev YI, *et al. The association of neuropsychiatric disorders and endocrine parameters in hashimoto thyroiditis. Pediatrician (St. Petersburg) 2020;11:55-68.*
5. Magy L, Vallat JM. *[Hashimoto's encephalitis]. Rev Neurol (Paris) 2002;158(10 Pt 1):966-970. French.*
6. Haggerty JJ Jr, Evans DL, Golden RN, Pedersen CA, Simon JS, Nemeroff CB. *The presence of antithyroid antibodies in patients with affective and nonaffective psychiatric disorders. Biol Psychiatry 1990;27:51-60.*
7. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. 5th ed. Arlington:American Psychiatric Publishing;2013.*
8. Aouizerate B, Guehl D, Cuny E, Rougier A, Bioulac B, Tignol J, *et al. Pathophysiology of obsessive-compulsive disorder: A necessary link between phenomenology, neuropsychology, imagery and physiology. Prog Neurobiol 2004;72:195-221.*
9. Endres D, Pollak TA, Bechter K, Denzel D, Pitsch K, Nickel K, *et al. Immunological causes of obsessive-compulsive disorder: is it time for the concept of an "autoimmune OCD" subtype? Transl Psychiatry 2022;12:5.*
10. Giynas Ayhan M, Uguz F, Askin R, Gonen MS. *The prevalence of depression and anxiety disorders in patients with euthyroid Hashimoto's thyroiditis: A comparative study. Gen Hosp Psychiatry 2014;36:95-98.*
11. Caykoylu A, Kabadayi Sahin E, Ugurlu M. *Could the thyroid gland dominate the brain in obsessive-compulsive disorder?*

Neuroendocrinology 2022;112:1143-1154.

12. Maina G, Albert U, Bogetto F, Borghese C, Berro AC, Mutani R, *et al. Anti-brain antibodies in adult patients with obsessive-compulsive disorder. J Affect Disord 2009;116:192-200.*
13. Müssig K, Künle A, Säuberlich AL, Weinert C, Ethofer T, Saur R, *et al. Thyroid peroxidase antibody positivity is associated with symptomatic distress in patients with Hashimoto's thyroiditis. Brain Behav Immun 2012;26:559-563.*
14. Abramowitz JS, Deacon BJ, Olatunji BO, Wheaton MG, Berman NC, Losardo D, *et al. Assessment of obsessive-compulsive symptom dimensions: Development and evaluation of the Dimensional Obsessive-Compulsive Scale. Psychol Assess 2010; 22:180-198.*
15. Şafak Y, Say Öcal D, Özdel K, Kuru E, Örsel S. *[Dimensional approach to obsessive-compulsive disorder: Dimensional Obsessive-Compulsive Scale with Turkish psychometric properties]. Turk Psikiyatri Derg 2018;29:122-130. Turkish.*
16. Ferracci F, Moretto G, Candeago RM, Cimini N, Conte F, Gentile M, *et al. Antithyroid antibodies in the CSF: Their role in the pathogenesis of Hashimoto's encephalopathy. Neurology 2003;60:712-714.*
17. Moodley K, Botha J, Raidoo DM, Naidoo S. *Immuno-localisation of anti-thyroid antibodies in adult human cerebral cortex. J Neurol Sci 2011;302:114-117.*
18. Endres D, Runge K, Meixensberger S, Feige B, Denzel D, Pankratz B, *et al. An observational study on the association of anti-thyroid autoantibodies with clinical, EEG, MRI, FDG-PET, cerebrospinal fluid and anti-neuronal antibody findings in 530 patients with schizophreniform and affective disorders. Psychoneuroendocrinology 2021;131:105320.*
19. Leyhe T, Hügle M, Gallwitz B, Saur R, Eschweiler GW. *Increased occurrence of severe episodes in elderly depressed patients with elevated anti-thyroid antibody levels. Int J Geriatr Psychiatry 2009;24:779-781.*
20. Eller T, Metsküla K, Talja I, Maron E, Uibo R, Vasar V. *Thyroid autoimmunity and treatment response to escitalopram in major depression. Nord J Psychiatry 2010;64:253-257.*
21. Oomen HA, Schipperijn AJ, Drexhage HA. *The prevalence of affective disorder and in particular of a rapid cycling of bipolar disorder in patients with abnormal thyroid function tests. Clin Endocrinol (Oxf) 1996;45:215-223.*
22. Bartalena L, Pellegrini L, Meschi M, Antonangeli L, Bogazzi F, Dell'Osso L, *et al. Evaluation of thyroid function in patients with rapid-cycling and non-rapid-cycling bipolar disorder. Psychiatry Res 1990;34:13-17.*
23. Ngo ST, Steyn FJ, McCombe PA. *Gender differences in autoimmune disease. Front Neuroendocrinol 2014;35:347-369.*
24. Vanderpump MPJ. *The epidemiology of thyroid diseases. In: Braverman LE, Utiger RD, editors. Werner and Ingbar's the thyroid: A fundamental and clinical text. 9th ed. Philadelphia:JB Lippincott-Raven;2005. p.398-496.*
25. Grönwall C, Akhter E, Oh C, Burlingame RW, Petri M, Silverman GJ. *IgM autoantibodies to distinct apoptosis-associated antigens correlate with protection from cardiovascular events and renal disease in patients with SLE. Clin Immunol 2012;142: 390-398.*
26. Özmen T, Güllüoğlu BM, Yegen CŞ, Soran A. *Autoimmune thyroid disease and breast cancer prognosis. J Breast Health 2015;11:67-71.*
27. Fröhlich E, Wahl R. *Thyroid autoimmunity: Role of anti-thyroid antibodies in thyroid and extra-thyroidal diseases. Front Immunol 2017;8:521.*