

Quality of Life and Mood Disorders in Patients with Hashimoto Thyroiditis

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Abstract: *Aim: It is well known that hypothyroidism is associated with poorer quality of life. Still, there are more studies nowadays that also report low health-related quality of life (HRQoL), more depression, and anxiety in euthyroid Hashimoto thyroiditis (HT). We hypothesized that autoimmunity itself is associated with low HRQoL and a high prevalence of mood disorders in euthyroid HT. Patients and methods: We examined 130 euthyroid patients with HT (90% females) and 111 matched euthyroid, healthy controls. The groups were subdivided per age: 20-49 yrs. and 50 years. We conducted a cross-sectional analysis. We took blood samples for thyroid hormone levels and thyroid autoantibodies. We examined HRQoL via the health questionnaire (SF-36) short-form version 1 and the presence and degree of mood disorders with the Hospital anxiety and depression scale (HADS) questionnaire. Significant associations between variables were examined with ANOVA analysis and partial correlations. Results: Patients were significantly more depressed than control subjects ($p < 0.001$), and have had more anxiousness, but only in the younger group ($p < 0.05$). Quality of life was significantly better in the older control group comparing to patients with Hashimoto ($p < 0.01$). The overall SF-36 score was in a significant negative correlation with antibodies (TPOAb, TgAb). Depression was positively associated with TSH and TPOAb levels. Conclusion: Our study indicated that euthyroid patients with HT had worse HRQoL and showed more symptoms of anxiety and depression. We also have found that levels of thyroid antibodies were crucial in terms of neuropsychological wellbeing. More studies with longitudinal observations could explain a possible causal relationship.*

Keywords: *research project; Hashimoto thyroiditis; thyroid; autoimmunity; quality of life; mood disorders.*

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Introduction

Hashimoto thyroiditis (HT) is autoimmune thyroiditis (AIT) and is the major cause of decreased thyroid hormone secretion in adult patients. The diagnosis of HT is made by a combination of positive circulating antibodies against thyroid with typical clinical signs, and special thyroid ultrasound characteristics (Caturegli, De Remigis & Rose, 2014). HT may lead to hypothyroidism, but there is a euthyroid stage of HT, too.

In the United States, the prevalence of AIT is approximately 4 % to 13 % (Canaris et al., 2000; Hollowell et al., 2002). The prevalence rates are higher in females than males, and rises with age, even up to 20% in elderly females (Surks et al., 2004). In addition, depression and anxiety disorders are also frequent in the general population (Siegmann et al., 2018). It is very important to be aware of associations between these three conditions because early diagnosis and adequate treatment are of public interest.

It is well known that hypothyroidism is associated with poorer quality of life (Winter et al., 2016). Still, there are more studies nowadays that also report low HRQoL, more depression, anxiety, sometime suicide in euthyroid HT (Fulga, Perju-Dumbrava & Crassas, 2008; Ott et al., 2011; Perju-Dumbrava et al., 2019). These findings were the starting point for our research. We hypothesized that autoimmunity itself is associated with low HRQoL and a high prevalence of mood disorders in euthyroid HT.

Patients and methods

The study was conducted at the Outpatient Clinic for Endocrinology, diabetes, and metabolic diseases, Clinical Centre of Serbia. We examined 130 patients (mean age 50.12 ± 13.93 years, 90% females) with HT. The inclusion criteria were that all patients were well controlled, namely, they had TSH in the reference range (0.27-4.20 mIU/L). In addition, we included 111 matched euthyroid, healthy controls. Two groups (patients with HT and the control group) were subdivided per age: 20-49 years and \square 50 years. We conducted a cross-sectional analysis.

We took blood samples for FT3, FT4, TSH, anti-Tg, anti-TPO, and other standard biochemical measurements. From a neuropsychological point of view, among other tests, we used the Short Form health questionnaire (SF-36) version 1 and the Hospital anxiety and depression scale (HADS). We performed ANOVA analysis and partial correlations to find significant associations. All tests were performed using SPSS software (version 17.0, SPSS Inc., Chicago, IL)

Results

Neuropsychological outcome:

Patients were significantly more depressed than controls ($p < 0.001$) in both age groups. Nevertheless, only in the younger group of patients with HT were found significantly more anxiousness ($p < 0.05$) comparing to the control participants at the same age. Total SF-36 scores were significantly higher in the older group of control participants comparing to older patients with HT ($p < 0.01$). *Table 1.*

Table 1. HRQoL and HADS in the subject subgroups

Groups	Age groups	HADSA	p	HADSD	p	HRQoL	p
Hashimoto (n=59)	20-49 yrs.	11.07±3.17	0.036*	9.31±3.79	0.003**	69.79±16.44	0.084
Controls (n=79)		9.65±3.07		7.10±2.82		76.42±14.13	
Hashimoto (n=71)	≥ 50 yrs.	10.11±4.30	0.086	10.76±4.13	0.005**	57.59±21.07	0.009*
Controls (n=32)		8.20±3.26		7.30±2.21		73.70±14.17	

HADSA, Hospital anxiety and depression scale – Anxiety; HADSD, Hospital anxiety and depression scale – Depression; HRQoL, Health-related quality of life (SF-36) scores. ANOVA: * $p < 0.05$; ** $p < 0.01$

We examined whether there are significant connections between thyroid hormone levels (TSH, FT4, FT3, FT4 / FT3) and the presence of antibodies (TPOAb, TgAb) with neuropsychological outcome measures. The overall SF-36 score was significantly negatively associated with antibodies (TPOAb, TgAb). Depression was positively associated with TSH and TPOAb levels. *Table 2.*

Table 2. Association of HRQoL, anxiety and depression with hormonal status and thyroid autoantibodies (partial correlations adjusted for age, education, BMI)

Antibodies	Partial correlation	HADSA	HADSD	HRQoL
TSH	Correlation (r)	- 0.053	0.238	- 0.069
	Sig. (p)	0.557	0.007*	0.535
TgAb	Correlation (r)	0.008	- 0.151	- 0.233
	Sig. (p)	0.926	0.090	0.034*
TPOAb	Correlation (r)	0.166	0.248	- 0.218
	Sig. (p)	0.063	0.005**	0.048*

TgAb, Thyroglobulin antibodies; TPOAb, thyroid peroxidase antibodies; HADSA, Hospital anxiety and depression scale – Anxiety; HADSD, Hospital anxiety and depression scale – Depression; HRQoL, Health-related quality of life; *p<0.05; **p<0.01

Discussion

In our study of 130 euthyroid patients with HT and 111 matched controls, we found a significant association between high antibodies levels and poor quality of life and depression independently of thyroid hormone levels. Our results are in agreement with other studies. There is a study from Dardano and colleagues where they hypothesized that thyroid autoimmunity is responsible for the presence of symptoms in euthyroid HT (Dardano et al., 2012). They found that patients on adequate levothyroxine replacement therapy with normal TSH showed the poorer quality of life. Consequently, some studies have implicated that thyroidectomy would make sense in terms of improving the quality of life in patients with HT (Zivaljevic et al., 2015). In a study by Mussig et al. (2012) high anti-TPO antibodies were associated with worse HRQoL, although all patients with HT were under levothyroxine treatment and were euthyroid (Mussig et al., 2012). Ott et al. (2011) examined female patients undergoing thyroid surgery for benign thyroid diseases. Euthyroid female patients with high anti-TPO levels had unfavorable HRQoL scores compared to euthyroid female patients with low anti-TPO levels. Some parts of HRQoL scores were significantly reduced in euthyroid female patients with high anti-TPO levels, for example, general health, role physical, vitality, social functioning, and mental health scores. They accentuated that patients with HT have reduced HRQoL scores

independently from hypothyroidism. Moreover, in another study by Yalcin and colleagues (2017), euthyroid patients with HT had worse HRQoL scores compared to the control group in particular segments of physical functioning, general health, and mental health (Perju-Dumbrava et al., 2013). There was a negative correlation between mental health, emotional scores, and anti-TPO levels. Watta et al. examined ThyPRO QoL scores from 199 outpatients with autoimmune hypothyroidism (2012). They hypothesized that physiological dysfunction through specifically related symptoms, was the cause of bad functioning and well-being, and consequently low QoL. In univariate regression analysis thyroid volume and hormone levels had no significant relationships with the ThyPRO QoL scales. On the contrary, TPOAb levels were related to symptoms and scales measuring wellbeing and function. In the multivariate analysis, TPOAb levels were related to goiter symptoms, depression, and anxiety. They concluded that the relationship between TPOAb and the ThyPRO QoL scales was probably associated with depression. Blanchin and colleagues showed that antibodies against TPO bind to human cerebellar astrocytes in patients with Hashimoto's encephalopathy (2007). Consequently, the presence of high thyroid autoantibodies may lead to some changes in the brain which may lead to poorer quality of life if compared with subjects without thyroid autoimmunity.

Marquez et al. found microvascular changes in the skeletal muscle of patients with autoimmune thyroiditis, independently of thyroid function (Marquez et al., 2001). They hypothesized that the same microvascular changes might be present in other tissues as well, including the central nervous system. That could be an explanation of the associations between autoimmunity and mental health.

There are studies that have examined the association between thyroid and brain function using positron emission tomography (Marangell & Callahan 1998), as well as studies that have found an association between therapy-resistant depression and hypothyroidism (Hendrick, Altshuler, L. & Whybrow, 1998). Nevertheless, in patients with autoimmune thyroiditis, no changes were found in certain regions of the brain that would be responsible for depressive disorder. A recent study by Leyhe and Müssig suggested some explanations (2014). Antibodies against TPO bind to human astrocytes and, presumably, may play a direct role in the pathogenesis of cognitive and affective disorders. Antibodies against the central nervous system were also found to be significantly increased in patients with HT. These antibodies disrupt myelinogenesis in vitro and, therefore, may impair the integrity of the myelin sheath. The production of inflammatory cytokines significantly

increases in patients with HT. Inflammatory cytokines negatively affect the synthesis, release, and reuptake of multiple neurotransmitters, such as serotonin, dopamine, and glutamate, resulting in changes in various brain pathways.

On the contrary, the study by Saravanan, Visser, and Dayan on more than 500 patients with HT on hormone replacement therapy found an association between psychological wellbeing and thyroid function, but not antibodies against TPO (2006). However, TPOAb was analyzed as a dichotomized, not a continuous variable, as revealed by our study, which could explain the observed difference.

Conclusions

Many studies have exposed that autoimmune thyroiditis is associated with depression and anxiety disorders. Therefore, it is important to increase the doctor's awareness of this connection in order to speed up the diagnostic process. In patients with depression and anxiety disorders, a test for HT should be performed, and in patients with HT, screening for psychiatric symptoms is recommended. Patients with autoimmune thyroiditis must be aware of the vulnerability to develop mood disorders. An appropriate and early treatment leading to better wellbeing and QoL would be a huge advantage for patients.

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