

# Thyroglobulin antibodies are associated with symptom burden in patients with Hashimoto's thyroiditis



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**Objectives:** Hashimoto thyroiditis (HT) is the most common form of autoimmune thyroid disorders, caused by antibodies to thyroglobulin (TgAb) and thyroid peroxidase (TPOAb). Today there is rising interest in influence of thyroid antibodies on human health. In our study we have included large cohort of patients with HT to investigate possible influence of thyroid autoimmunity on symptom burden.

**Methods:** In the period from 2013 to 2017 we collected data from 290 HT patient at the Department for Nuclear Medicine at the University Hospital Split, including 270 females (93%) and 20 males (7%). We collected information on thyroid-specific phenotypes (TSH, T3, T4, fT4, TgAb, TPOAb, thyroid volume) and other clinical phenotypes (age, body surface area, number of hypothyroidism symptoms, blood pressure) from patients with HT without levothyroxine (LT4) therapy.

**Results:** We have analysed correlations between thyroid-specific and other clinical phenotypes (Table 1). The most frequently reported symptom was weakness (63%), and the rarest symptom was slow speech (Figure 1). We have found significant positive correlation between TgAb levels and the number of symptoms ( $r=0.25$ ,  $P=0.0001$ ) in HT patients that remained significant after adjustment for TPOAb, T3, TSH levels and thyroid volume ( $\beta=0.66$ ,  $SE=0.3$ ,  $P=0.0299$ ). Increased TgAb levels are significantly associated with fragile hair ( $P=0.0043$ ), face edema ( $P=0.0061$ ), edema of the eyes ( $P=0.0293$ ) and harsh voice ( $P=0.0349$ ) (Figure 2.).

**Conclusions:** TgAb have important effect on general health and clinical manifestations of HT, and elevated TgAb level may cause the observed symptom burden in HT patients, leading to conclusion that not all HT patients may be clustered in one group. Based on these results, we recommend screening for TgAb antibodies in HT patients with symptom burden. The symptoms in patients with HT should be further differentiated to those that are truly caused by hypothyroidism and those that develop due to autoimmunity per se.

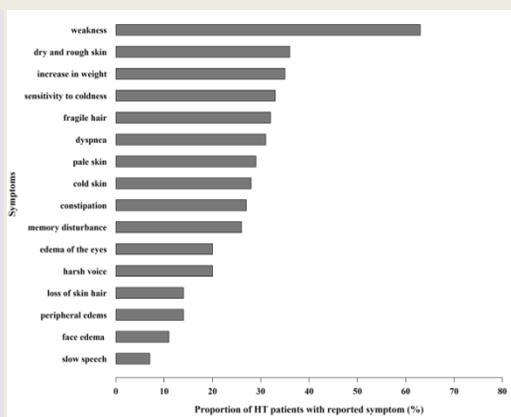


Figure 1. Frequencies of appearance of hypothyroidism symptoms in HT patients.

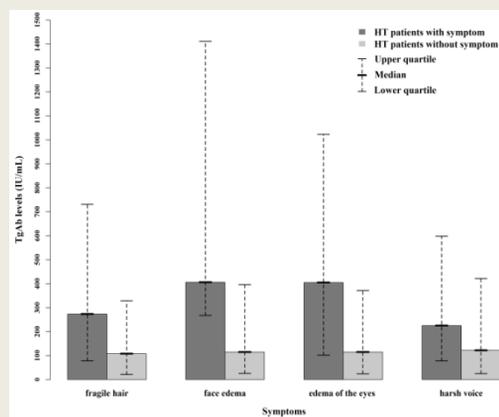


Figure 2. Comparison of median TgAb levels between HT patients with and without each of the four TgAb-associated symptoms.

Table 1. Correlation between thyroid-specific phenotypes and other clinical phenotypes.

		Age	BSA	Number of symptoms	Systolic blood pressure	Diastolic blood pressure
TSH	r	0,17	0,17	0,11	0,23	0,22
	P	<b>0,0054</b>	<b>0,0062</b>	<b>0,0932<sup>2</sup></b>	<b>0,0013</b>	<b>0,0030</b>
T3	r	0,02	-0,06	-0,15	0,00	0,08
	P	0,7812	0,2887	<b>0,0238<sup>2</sup></b>	0,9518	0,2793
T4	r	0,00	-0,03	-0,11	-0,05	-0,01
	P	0,9520	0,5696	0,0880	0,5417	0,8472
fT4	r	-0,21	-0,12	-0,10	-0,14	-0,08
	P	<b>0,0004</b>	0,0573	0,1314	0,0629	0,2665
TgAb	r	0,01	0,07	0,25	-0,05	0,03
	P	0,8108	0,2190	<b>0,0001<sup>2</sup></b>	0,4700	0,7080
TPOAb	r	0,10	0,06	0,19	0,10	0,12
	P	0,0956	0,2939	<b>0,0034<sup>2</sup></b>	0,1603	0,1106
Thyroid volume	r	0,01	0,18	0,16	0,03	0,08
	P	0,8800	<b>0,0028</b>	<b>0,0193<sup>2</sup></b>	0,6709	0,3117

P-values less than Bonferroni corrected value of 0.0071 (0.05/7) are bolded.

r-Spearman rank correlation coefficient, P-p-value

<sup>2</sup>After including these five phenotypes in linear regression model for the number of symptoms, only TgAb levels remained significantly associated with the number of symptoms ( $\beta=0.66$ ,  $SE=0.3$ ,  $P=0.0299$ ).