International Journal of Research in Medical Sciences
Baştuğ BT. Int J Res Med Sci. 2016 May;4(5):1433-1437
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20161205

Research Article

If this argument is true: Hashimoto's disease causes chronic thyroid damage so in diseased elderly population the thyroid volumes must be low-retrospective US study

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Received: 16 February 2016
Revised: 21 February 2016
Accepted: 22 March 2016

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ABSTRACT

Background: Hashimoto thyroiditis is part of the spectrum of autoimmune thyroid diseases and is characterized by the destruction of thyroid cells by various cell and antibody-mediated immune processes. It primarily affects middle-aged women but also can occur in men and children. Hashimoto's disease typically progresses slowly over years and causes chronic thyroid damage. This has to be thought that in diseased elderly population the thyroid volumes must be low. This paper shows if this argument is true and how thyroid volumes change over years by the disease Hashimoto because of chronic thyroid damage. A review of the literature revealed several studies about thyroid volume changes by aging and by Hashimoto thyroiditis separately. But there has not been any study in literature wondering how thyroid volumes change by aging in the course of the disease Hashimoto.
Methods: The study was designed as a retrospective investigation. The study group included 136 patients who admitted for sonography examination between the years 2012-2014 whom have suffered from Hashimoto's disease. In the study, control groups were formed with 73 healthy individuals who volunteered for participation. The volume of each thyroid lobe was calculated with ellipsoid formula: (volume (ml) = Length (cm) x Width (cm) x Thickness (cm) x1/6 Л).
Results: While healthy individuals are grown older, thyroid volumes are increased. In diseased individuals while aging although disease causes chronic thyroid damage, volume measurements do not change.
Conclusions: The results have suggested that while aging although disease causes chronic thyroid damage, volume measurements do not change. Because volume reduction due to chronic damage of disease is balanced by volume increase due to aging.

Keywords: Hashimoto's thyroiditis, Chronic thyroid damage, Thyroid volumes, US

INTRODUCTION

Hashimoto's thyroiditis or chronic lymphocytic thyroiditis is an autoimmune disease in which the thyroid gland is attacked by a variety of cell- and antibody-mediated immune processes.[1] It was the first disease to be recognized as an autoimmune disease.[2] The resulting inflammation from Hashimoto's disease, also known as chronic lymphocytic thyroiditis, often leads to an underactive thyroid gland (hypothyroidism). The thyroid gland may become firm, large, and lobulated in Hashimoto's thyroiditis or changes in the thyroid can also be nonpalpable and this is based on lymphocytic infiltration and fibrosis rather than tissue hypertrophy.

Also Hashimoto's disease typically progresses slowly over years and antibodies against thyroid peroxidase (TPO) and/or thyroglobulin cause gradual destruction of follicles in the thyroid gland leading to a drop in thyroid hormone levels in your blood. Initially because of lymphocytic infiltration thyroid gland may be large but when normal thyroid cells are destroyed over years then thyroid gland may become smaller. A review of the literature revealed several studies about thyroid volume changes by aging and by Hashimoto thyroiditis separately. But there has not been any study in literature wondering how thyroid volumes change by aging in the course of the disease Hashimoto.

METHODS

The study was designed as a retrospective investigation. The study group included 136 patients who admitted to Bilecik State Hospital, Radiology Department for sonography examination between the years 2012-2014 whom have suffered from Hashimoto's disease. In the study, control groups were formed with 73 healthy individuals who volunteered for participation. GE Logiq P5 USG device with 10 MHz linear probe in Bilecik State Hospital Radiology Department was used. In our study individuals were subdivided into 3 groups according to age (0-29, 30-49 and over 50), 2 groups according to gender (45 male and 164 female) and into 2 groups depending on whether diseased or not. Craniocaudal length, transverse and mediolateral length (width), anteroposterior length for each lobe and isthmus thickness were included in the work.

The volume of each thyroid lobe was calculated with ellipsoid formula: (Volume (ml) = Length (cm) x Width (cm) x Thickness (cm) x 1/6 JI).

Total volume was obtained as the sum of two thyroid lobes. The isthmus was not included into the sum.

RESULTS

In statistical analysis, the correlation between sex and thyroid volumes (right and left lobe volumes, and total volume) were evaluated with independent-samples T test. In Table 1, mean thyroid volumes are summarized according to sex. All the thyroid volumes are bigger in men than in women. $p<0.05$ was accepted statistically significant (Table 1).

The correlation between Hashimoto's thyroiditis and thyroid volumes (right and left lobe volumes, and total volume) were evaluated with independent-samples T test. In Table 2, mean thyroid volumes are summarized according to disease. All the thyroid volumes are smaller in diseased individuals than in healthy ones. $p<0.05$ was accepted statistically significant (Table 2).

Altough the individuals whom large nodule were discovered have created a very small number (6/209) of total, the thyroid volumes were found bigger than others. But because of small size statistical analysis were not rational (Table 3).

Table 1: All the thyroid volumes are bigger in men than in women.

Gender		N	Mean	Std. deviation	t value	p value
Right lobe	Female	164	2.5385	1.51396	-3.56635	0.001
	Male	45	3.3449	1.29301		
Left lobe	Female	164	2.1888	1.24766	-2.40147	0.018
	Male	45	2.5824	0.88415		
Total volume	Female	164	4.7136	2.50657	-3.49530	0.001
	Male	45	5.9096	1.88266		

Table 2: All the thyroid volumes are smaller in diseased individuals then healthy ones.

Hashimoto's disease		N	Mean	Std. deviation	t value	p value
Right lobe	Positive	136	2.7204	1.69024	0.10915	0.91319
	Negative	73	2.6966	1.08282		
Left lobe	Positive	136	2.2404	1.31919	-0.54961	0.58318
	Negative	73	2.3353	0.89937		
Total volume	Positive	136	4.9382	1.73397	-3.44430	0.0001
	Negative	73	5.2323	1.75229		

To investigate the relationship between the measured values according to age group, partial correlation analysis was performed. According to the results, it is seen that there is a significant correlation between the left, right

and the total volume value according to age groups (p<0,05). While the ages grow, volume measurements are increased, but this increase is not linear (0-29, 30-39 and over 50) (Table 4).

Table 3: The thyroid volumes were found bigger than others.

Nodule positive		N	Mean	Std. Deviation	t value	p value
Right lobe	Positive	6	7.2500	2.71790	8.76275	0.00000
	Negative	203	2.5780	1.23077		
Left lobe	Positive	6	4.6500	1.85984	5.28318	0.00000
	Negative	203	2.2033	1.09323		
Total volume	Positive	6	11.9000	2.08710	8.10732	0.00000
	Negative	203	4.7663	2.12507		

Table 4: While the ages grow, volume measurements are also increase, but this increase is not linear.

Control value			Right lobe	Left lobe	Total volume
Age groups	Right lobe	r	1.000	0.638	0.924
		p	-	0.000	0.000
	SLeft lobe	r	0.638	1.000	0.880
		p	0.000	-	0.000
	Total Volume	r	0.924	0.880	1.000
		p	0.000	0.000	-

The correlation between aging in the course of disease and thyroid volumes (right and left lobe volumes, and total volume) was evaluated with one-way multivariate analysis of variance test. Initially, aging and disease effect on volumes were evaluated separately. Then total effect (aging in the course of disease) was summarized. While the presence of disease have had effect (p<0.05), aging in the course of disease have had no effect on volumes (p>0.05) (Table 5).

For determination the variables which cause individuals to be diseased, logistic regression application has done. Logistic regression model has done with age, gender and total volume variables. Gender and total volume was found to be independent risk factors affecting the disease states. If the meaningful variables are interpreted, possibility of illness in female patients increases about 6.78 times (%95 CI 2,639-16,654) than in male patients. And also a one-unit decrease in the value of total volume increases possibility of illness 3.22 times (1,555-11,25). With the variables of model, at least 20% of the disease states are disclosed and the overall success rate of the model was 93.3% (Table 6).

Table 5: While the presence of disease have had effect (p<0.05), aging in the course of disease have had no effect on volumes.

Source	Type III sum of squares	Df	Mean square	F value	P value
Corrected Model	410.208[a]	14	29.301	6.929	0.000
Intercept	2418.824	1	2418.824	572.007	0.000
Age	11.785	2	5.893	1.394	0.251
Disease	17.942	1	17.942	5.223	0.001
Age * disease	4.894	2	2.447	0.579	0.562

Table 6: The overall success rate of the model was 93.3%.

Model	Wald	p	Odds ratio	%95 CI lower limit	%95 CI upper limit
Gender	8.930	*0.003*	6.777	2.639	16.654
Age	0.587	0.444	1.811	0.396	8.280
Total Volume	6.442	*0.011*	3.222	1.555	11.25
Model Chi-square: 34.101; -2LL=54.326; sd: 4; n=150; p<0.001; Success rate= %93.3; Cox & Snell R^2= 0.203; Nagelkerke R^2= 0.457.					

All the thyroid volumes are bigger in men than in women. p<0.05 was accepted statistically significant. All the thyroid volumes are smaller in diseased individuals then healthy ones. p<0.05 was accepted statistically significant. Although the individuals whom large nodule

were discovered have created a very small number (6/209) of total, the thyroid volumes were found bigger than others. While the ages grow in healthy individuals, volume measurements are increase, but this increase is not linear ($p<0.05$). The correlation between aging in the course of disease and thyroid volumes shows that while the presence of disease have had effect on volumes ($p<0.05$), aging in the course of disease have had no effect $p>0.05$).These results have suggested that while getting older volume reduction due to disease is balanced by volume increase due to aging. Although individuals are diseased, chronic damage cannot effect volume measurements according to volume increase due to aging.

DISCUSSION

Hashimoto's thyroiditis or chronic lymphocytic thyroiditis; is an autoimmune disease in which the thyroid gland is attacked by a variety of cell- and antibody-mediated immune processes.[1] It was the first disease to be recognized as an autoimmune disease.[2] Hashimoto's thyroiditis is named after the Japanese physician Hakaru Hashimoto (1881−1934) of the medical school at Kyushu University, who first described the symptoms of patients with struma lymphomatosa, an intense infiltration of lymphocytes within the thyroid, in 1912.[3]

The resulting inflammation from Hashimoto's disease, also known as chronic lymphocytic thyroiditis, often leads to an underactive thyroid gland (hypothyroidism). This disorder is believed to be the most common cause of primary hypothyroidism in North America; as a cause of non-endemic goiter, it is among the most common.[4] Patients usually present with hypothyroidism ± a goiter. However a very small proportion of cases (~5%) can present with hyperthyroidism (hashi thyrotoxicosis). An average of 1 to 1.5 in 1000 people has this disease. Because of that hypothyroidism fatigue, weight gain, pale or puffy face, feeling cold, joint and muscle pain, constipation, dry and thinning hair, heavy menstrual flow or irregular periods, depression, a slowed heart rate, and problems getting pregnant and maintaining pregnancy can be seen in those patients.

Typically affects middle aged females (30-50 year age group with a F:M ratio of ~ 10-15:1). It is more common in regions of high iodine dietary intake, and among people who are genetically susceptible.

There are multiple suggested mechanisms by which the pathology of Hashimoto's thyroiditis develops. Various autoantibodies may be present against thyroid peroxidase, thyroglobulin and TSH receptors; although a small percentage of patients may have none of these antibodies present. And also a percentage of the population may also have these antibodies without developing Hashimoto's thyroiditis. Nevertheless, antibody-dependent cell-mediated cytotoxicity is a substantial factor behind the apoptotic fall-out of Hashimoto's thyroiditis. Activation of cytotoxic T-lymphocytes in response to cell-mediated immune response affected by helper T-lymphocytes is central to thyrocyte destruction. And another way is lymphocytes producing inflammatory cytokines within thyroid tissue to further macrophage activation and migration into the thyroid gland for direct effect. Diagnosis is usually made by detecting elevated levels of anti-thyroid peroxidase antibodies in the serum, but seronegative (without circulating autoantibodies) thyroiditis is also possible.

The thyroid gland may become firm, large, and lobulated in Hashimoto's thyroiditis, but changes in the thyroid can also be nonpalpable. Enlargement of the thyroid is due to lymphocytic infiltration and fibrosis rather than tissue hypertrophy. Physiologically, antibodies against thyroid peroxidase (TPO) and/or thyroglobulin cause gradual destruction of follicles in the thyroid gland.

It is difficult to reliably sonographically differentiate Hashimoto thyroiditis from other thyroid pathology. Ultrasound features can be variable depending of the severity and phase of disease.[5,6] Diffusely enlarged thyroid gland with a heterogeneous echo texture is a common sonographic presentation.[7] Presence of hypo echoic micronodules (1-6mm) with a surrounding echogenic septations is also considered to have a relatively high positive predictive value.[8,9] Color Doppler study usually shows normal or decreased flow but occasionally there might be hyper vascularity similar to thyroid gland. In some situations, large nodules may be present which named nodular Hashimoto thyroiditis. [10] In differential diagnosis ultrasound appearances consider lymphoma affecting thyroid gland, papillary thyroid carcinoma and subacute granulomatous (de Quervain) thyroiditis.

A review of the literature revealed several studies about thyroid volume changes by age.

Hegedüs L studies have demonstrated that the ultrasonic evaluation of thyroid volume is both accurate and precise. In addition, it is non-invasive, rapid, inexpensive and without discomfort to the patient. Using this technique it was demonstrated that thyroid volume increases with increasing age in both sexes similar to our study.[11]

Dvorakova M et al showed age-related increase of the volume of thyroid gland at both sexes somewhat similar to our study (F-ratio = 1.99, $p<0.0001$). Their results have demonstrated that at men and women the volume of thyroid gland fluently increases to the 30th year equally, from 30 years to 55 years it increases more rapidly in men while in women there is observed a moderate plateau. Further increase of the volume of thyroid gland is equally fluent from the age of 55 years.[12]

Barrere X et al found thyroid volume (ml) was correlated negatively with age for females ($P = 0.0009$) as opposed to our work.[13]

But there has not been any study in literature wondering how thyroid volumes change by aging in the course of the disease Hashimoto.

CONCLUSION

In this work we showed that all the thyroid volumes are bigger in men than in women. All the thyroid volumes are smaller in diseased individuals then healthy ones. While the ages grow in healthy individuals, volume measurements are increase. The correlation between aging in the course of disease and thyroid volumes shows that while the presence of disease separately have had effect on volumes ($p<0.05$), aging in the course of disease have had no effect ($p>0.05$). The results have suggested that the volume reduction due to disease is balanced by volume increase due to aging.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Baştuğ BT. If this argument is true: Hashimoto's disease causes chronic thyroid damage so in diseased elderly population the thyroid volumes must be low-retrospective US study. Int J Res Med Sci 2016;4:1433-7.