

## Characteristics of our patients with Hashimoto thyroiditis

Elif Özsu, Rahime Gül Yeşiltepe Mutlu, Filiz Çizmeci, Şükrü Hatun

Kocaeli University Medical Faculty, Department of Pediatrics, Division of Pediatric Endocrinology, Kocaeli, Turkey

### Summary

**Aim:** Hashimoto's thyroiditis (HT) is the most common cause of goitre and acquired hypothyroidism in children and adolescents. We aimed to investigate the clinical manifestations, epidemiological and laboratory characteristics of the patients with HT.

**Material and Method:** We reviewed files of 106 children and adolescents with HT followed up in the Department of Pediatric Endocrinology between January 2004 and December 2009. The patients were classified in four groups with respect to their thyroid function.

**Results:** Female patients constituted 78% (n=83) of all patients. Hashimoto's thyroiditis was 3.6 times more common in female patients. Mean age at diagnosis was 11.5±2.8 years. At the time of diagnosis 42.5% of patients (n:45) were euthyroid, 24.5% (n:26) had subclinical hypothyroidism, 29% (n:31) had overt hypothyroidism and 2.8% (n:3) had subclinical hyperthyroidism. The most common complaint at presentation was goitre which was observed in 49 (46%) children. Twenty six percent of all patients were admitted with growth retardation, 13% with weight gain, 6.4% with weight loss and 5.5% with nervousness. Familial history of thyroid disease was positive in 38 (35.8%) children. There were 28 patients (26.4%) in whom the disease was associated with another autoimmune disease. The most common concomitant autoimmune disease was type 1 diabetes mellitus (DM) (21.7%). Two patients (1,9%) had both type 1 diabetes mellitus and celiac disease and one patient (1%) had vitiligo.

**Conclusions:** We must investigate HT periodically in patients with autoimmune diseases because of increased risk. (*Turk Arch Ped* 2011; 46: 244-7)

**Key words:** Hashimoto thyroiditis, autoimmunity, adolescent

### Introduction

Hashimoto thyroiditis is the most common cause of goitre and acquired hypothyroidism in children and adolescents. It is an organ-specific autoimmune disease characterized by lymphocytic infiltration of the thyroid gland in which varying degrees of cellular and humoral immune response are involved and which results in thyroid cell death via apoptosis (1-3).

It is observed 2-4 times more frequently in girls compared to boys. The most common clinical findings are goitre and short stature. It makes a peak in the adolescence. Patients may present with clinical findings of symptomatic hypothyroidism, overt hypothyroidism and rarely hyperthyroidism (3-4). In this article, we aimed to present the clinical, epidemiological and laboratory findings of our patients with Hashimoto thyroiditis.

### Material and Method

106 patients aged 4.6-17.5 years old who were followed up in our clinic between January 2004 and December 2009

were evaluated. Age, gender, complaints at presentation, familial history and clinical and laboratory findings were recorded. Thyrotropin (TSH), thyroid hormone (triiodothyronine and thyroxine) levels and autoantibodies (anti-thyroglobulin and anti-peroxidase) were measured by chemulminescence. Thyroid ultrasonography was performed using "Ultrasound Toshiba Prime Ultrasound" device and 5Mhz probes. Urinary iodide level could not be measured. Thyroid scintigraphy was performed, if necessary using "Philips Adac" and technetium 99-m. Patients were divided in four groups according to thyroid function: euthyroid (both fT4 and TSH in normal limits), subclinical hypothyroidism (normal fT4, high TSH), overt hypothyroidism (low fT4, high TSH) and subclinical hyperthyroidism (normal fT4, suppressed TSH).

For statistical analysis SPSS (version 13) was used. Differences between groups were determined using independent student's t test for tests with variables and Mann-Whitney U test for non-variable tests. Frequencies were compared using chi-square test. A p value of <0.05 was considered to be statistically significant.

**Address for Correspondence:** Elif Özsu MD, Kocaeli University Medical Faculty, Department of Pediatrics, Division of Pediatric Endocrinology, Kocaeli, Turkey

elozdr@gmail.com **Received:** 12.12.2010 **Accepted:** 31.03.2011

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### Results

75% of the patients (n=83) were female and 22% (n:23) were male. Hashimoto throiditis was found with a 3.6 fold higher rate in girls. Mean age at the time of diagnosis was 11.5±2.8 years. 72% of the patients (n:77) were in the puberty (Graphic 1-2).

The most common complaint at presentation was goitre (46%). This was followed by short stature (26%), weight gain (13%), nervousness (5.5%), palpitation (2.8%) and constipation (3.7%).

At the time of diagnosis, 42.5% of the patients were euthyroid, 24.5% had subclinical hypothyroidism, 29.2% had overt hypothyroidism and 2.8% had subclinical hyperthyroidism. When thyroid functions were compared by gender, the frequency of subclinical hypothyroidism and overt hypothyroidism was found to be 86% (n:50) in girls and 7.5% (n:8) in boys. The frequency of hypothyroidism was found to be higher in girls compared to boys and this difference was found to be statistically significant (p<0.05). There was no significant difference between the groups in terms of age, gender and the frequency of goitre (Table I).

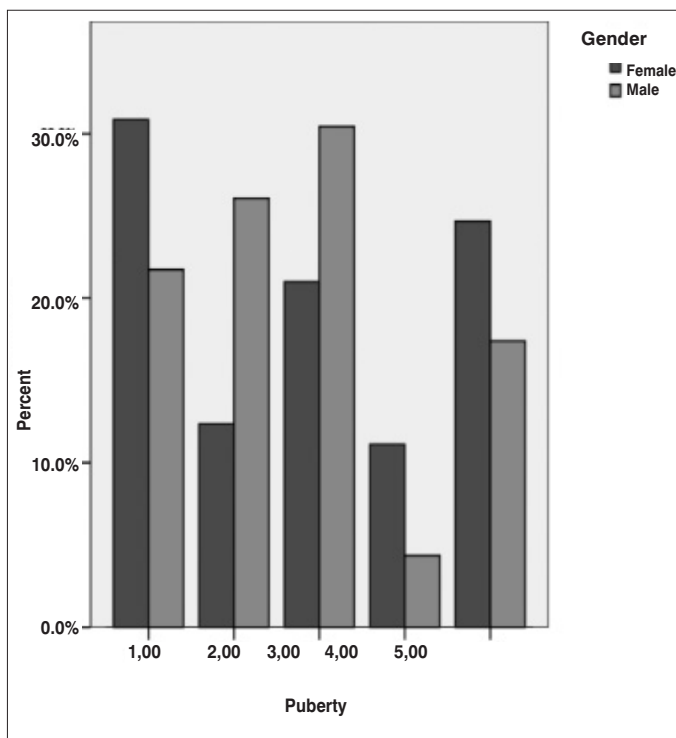
Mean anti-TPO level was found to be 353 IU/ml (2-1576 IU/ml) and mean anti-TG level was found to be 760 IU/ml

(4.7-7288 IU/ml). There was no statistically significant difference between hypothyroidic and euthyroidic patients in terms of autoantibodies (>0.05). There was no statistically significant difference between the groups with overt hypothyroidism and subclinical hypothyroidism in terms of autoantibody positivity (p>0.05).

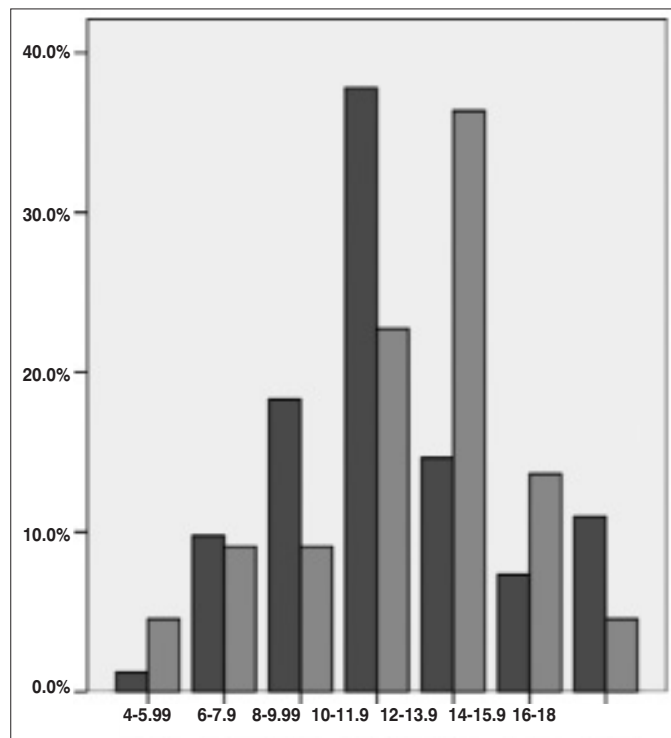
The frequency of thyromegaly was found to be 67% (n=39) in patients with hypothyroidism and 51%(n=23) in euthyroid patients. No statistically significant difference was found between the groups.

No significant difference was found between the groups with hypothyroidism in terms of body mass index.

Thyroid ultrasonography was performed in 81% of the patients (n=86) at the time of diagnosis. 64% of them had findings compatible with chronic thyroiditis, 5.8% had nodules, 8.7% were normal and 3.8% had chronic thyroiditis and nodules together. Thyroid functions in 10 patients with thyroid nodules were as follows: three were euthyroid, three had subclinical hypothyroidism and four had overt hypothyroidism. In 9 of the patients, thyroid scintigraphy was performed. Hyperplasic thyroid gland was found in 5 of them and a hypoactive nodule was found in four of them one of whom was found to have colloid nodule as a result of fine needle aspiration biopsy.



Graphic 1: Distribution of the patients by age



Graphic 2: Distribution of the patients by pubertal state

	Euthyroid N=45	Subclinical hypothyroidism N=27	Overt hypothyroidism N=31	Subclinical hyperthyroidism N=3	p
Age (years)	12.2±3.0	11.5±2.2	10.4±2.6	11.4±5	0.21
Gender (female/male)	30/15	23/4	27/4	3/0	0.08
Frequency of goitre	51%	62%	70%	100%	0.16

Treatment was not started in 25.5% of the patients (n=27) and L-thyroxine was started in 74.5% of the patients (n=79). Mean treatment time was 23±17 months (1-76 months). In follow-up, thyroid functions converted most frequently from hypothyroidism to euthyroid state (52.9%) and persisted as euthyroidic (34%) in the second order. In 6 patients, iatrogenic hyperthyroidism developed.

In 28 patients (26.4%), another autoimmune disease was present accompanying Hashimoto thyroiditis. Type 1 diabetes (DM) was the most common autoimmune disease with a rate of 21.7%. In two patients, celiac disease and DM were present in association and vitiligo was found in one of our patients.

When familial histories were evaluated, a familial history of thyroid disease was found in 35.8% of the patients (n=38). These included simple goitre (73.6%), Hashimoto thyroiditis (13.2%), Graves's disease (7.9%), thyroid nodule (5.3%) and hyperthyroidism without goitre (2.6%). When other accompanying autoimmune diseases were examined, type 1 DM was found in one person.

## Discussion

Hashimoto thyroiditis (chronic lymphocytic thyroiditis) is the most common disease of the thyroid gland in children and adolescents and the leading cause of acquired hypothyroidism and goitre in regions without endemic iodide deficiency. The disease is caused by increased T-cell activation and HLA tissue groups are related to development of goitre and thyroiditis. HLA-DR 4, HLA-DR5 cause to development of goitre and HLADR3 is responsible of atrophic thyroiditis (1-4).

Although the disease rarely occurs in the first three years of life, its frequency increases after the age of 6 and reaches the peak frequency in adolescence. In studies performed in our country, the mean age at the time of diagnosis was reported to be 11.4±2.97 years by Demirbilek et al. (4) and 12.4±2.97 years by Yeşilkaya et al. (15). In our study, the mean age at the time of diagnosis was found to be 11.5±2.8 years which was compatible with the literature (4-5).

Hashimoto thyroiditis is observed with a 2-4 fold increased frequency in girls. Many studies performed have reported ratios ranging between 2.1 and 8.7. In our study, female/male ratio was found to be 3,6 which was compatible with the literature (3,6).

Goitre is the most common complaint at the time of presentation (1-6). Its incidence is 40-70% and it was found to be 46% in our study. In a study performed in Israel, 40% of the patients were presented with goitre, 28.9% presented with symptoms of hypothyroidism, 12% referred to a doctor because of another reason and 10% was diagnosed as a result of investigations performed because of being in a high-risk group in terms of autoimmunity (7). In the study performed by Demirbilek et al. (4), goitre was observed in 55% of the patients and 18.6% of the patients presented with signs of hypothyroidism (short stature, weight gain). 11.1% of the patients were diagnosed during routine physical

examination (3). In our study, 24% of the patients (n:26) were found to have goitre during physical examination and referred to us. Other complaints at presentation included short stature (26%), weight gain (13%), nervousness (5.5%), palpitation (2.8%) and constipation (3.7%). In the study performed by Markoviç et al.(8), the rates of short stature, weight gain, increase in appetite, weakness and menstrual complaints were found to be 4.7%, 7%, 9.7%, 16% and 6.7% (8), respectively.

At the time of diagnosis, thyroid function tests were normal or subclinical hypothyroidism was present in most patients and the reason of goitre in these patients was lymphocytic infiltration or immunoglobulins enlarging thyroid tissue. While 78% of our patients had subclinical hypothyroidism or were euthyroidic, this rate was found to be 68% in another study performed in our country and 63% in the study performed by De Vies et al.(7) (3,7).

In our study, it was found that 54% of our subjects converted from hypothyroidism to euthyroidic state and 34% remained euthyroidic from the beginning. Spontaneous remission has been reported during the clinical course of the disease with a rate of 30-50% (2). In a study performed in Hacettepe University, 77% of the euthyroid patients remained euthyroid during follow-up, 69.5% of the patients with hypothyroidism persisted to have hypothyroidism and 30,5% of the patients with hypothyroidism were found to have entered remission. This suggests that Hashimoto thyroidism has a dynamic course and thyroid functions should be monitored periodically (9).

In a large-scale study demonstrating the association of autoimmune diseases, 1419 children with type 1 DM were investigated to determine the frequency of Hashimoto disease and a significantly higher frequency of thyroiditis was found compared to the normal population (3.9% compared to the frequency of 1.2% in the normal population in USA) (10). In our study, the most common accompanying autoimmune disease was type 1 DM and it was observed with a rate of 21%. This result suggests that attention should be paid to goitre in routine physical examination of patients with type 1 DM and autoantibody levels should be measured at regular intervals.

Hashimoto disease is observed with a rate of 10% and type 2 DM is observed with a rate of 70% as a component of type 1 autoimmune polyglandular syndrome (OPS). Association with pernicious anemia, alopecia, Addison's disease and vitiligo has been found (11). Celiac disease was found in two of our patients and vitiligo was found in one. Care should be taken in terms of OPS in the follow-up of these patients (11).

The frequency of Hashimoto disease is increased in some chromosomal diseases. For example, patients with Down, Klinefelter and Turner syndrome should be evaluated in this context. Association of Down syndrome, type 1 DM and Hashimoto thyroiditis was present in one of our patients who was 9 years old. None of our patients had Turner syndrome. Popva et al.(12) performed a study in 38 children

with Down syndrome in 2008 and found high levels of thyroid autoantibodies in 36 of them. Although goitre was found on physical examination in 6 of these patients, subclinical or overt hypothyroidism was found in 36 (12). In another study, the frequency of Hashimoto disease was found to be increased as the age advanced in patients with Turner syndrome and the frequency of autoimmune diseases was found to be increased 2 fold compared to the normal population (15% in the first decade and 30% in the third decade) (13).

Genetic predisposition and familial history with a rate up to 40% have been found in Hashimoto disease (1,2). Markoviç et al.(8) found familial history to be 37% in their study. Sengi et al.(14) reported that 58% of the mothers and 26% of the fathers were affected. In our study, autoimmune thyroid disease was found with a rate of 21% in families.

Although thyroid ultrasonography is not needed for diagnosis, a hypoechoic, diffuse, enlarged thyroid gland with a heterogenous property is observed when USG is performed (7). In 81% of our patients (n:86) thyroid ultrasonography was performed at the time of diagnosis. Findings compatible with chronic thyroiditis were found in 64% of them.

Fine needle aspiration biopsy should be performed in patients who develop nodule in follow-up and whose nodules do not regress with treatment. In the study performed by Demirbilek et al. (4), papillary thyroid cancer was found in one patient and surgery was performed. In our patients, the largest nodule found was 5 mm and the nodules disappeared or did not enlarge during follow-up. Since none of our patients had nodules that failed to regress or a nodule with a diameter more than 1 cm, fine needle aspiration biopsy was not performed in any of our patients. However, one of our patients whose goitre size was not reduced with drug treatment was referred to surgery because of anxiety about external appearance and histopathological evaluation was compatible with chronic lymphocytic thyroiditis. It is known that hypoactive nodules may be present on scintigraphy in Hashimoto thyroiditis (7).

Filipovic et al.(15) showed that lymphocytic thyroiditis was a risk factor for development of thyroid cancer and spread and hematogenous metastasis of cancer (15). One of the most important complications of Hashimoto disease is lymphoma (16-20). In a study performed in Korea which included adults, malignancy developed on the background of Hashimoto thyroiditis in 56% of 44 subjects with thyroid lymphoma. None of our patients was diagnosed as lymphoma or papillary thyroid cancer (16).

Consequently, thyroid function tests should be evaluated at regular intervals in Hashimoto thyroiditis which arises from autoimmunity and which has an increasing incidence as the age advances and it should be kept in mind that thyroid lymphoma and papillary thyroid cancer may accompany, though rarely.

**Conflict of interest: None declared.**

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