Zeynep Kamil Med J 2024;55(2):67–70
DOI: 10.14744/zkmj.2023.58751

ORIGINAL ARTICLE

Clinical features in children and adolescents with Hashimoto's thyroiditis

[1]Didar ARSLAN
[2]Feyza Mediha YILDIZ
[3]Heves KIRMIZIBEKMEZ

[1]Department Pediatric Intensive Care, Uludağ University Faculty of Medicine, Bursa, Turkey

[2]Department of Pediatrics, University of Health Sciences, Turkey. Istanbul Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center, Istanbul, Turkey

[3]Department of Pediatric Endocrinology, Ümraniye Training and Research Hospital, Istanbul, Turkey

ORCID ID
DA : 0000-0002-1730-0005
FMY : 0000-0002-8684-0101
HK : 0000-0002-8663-3452

ABSTRACT

Objective: Hashimoto's thyroiditis (chronic autoimmune thyroiditis) is the most common cause of goiter and acquired hypothyroidism among children and adolescents. It is an autoimmune disease intrinsic to thyroid tissue. In our study, we aim to review the files of children and adolescents with Hashimoto's thyroiditis, being followed up in the Department of Pediatric Endocrinology, and to compare these results with findings in the literature.

Material and Methods: In the study, the files of 114 children and adolescents with Hashimoto's thyroiditis, being followed up in Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center, Pediatric Endocrinology Department, were reviewed retrospectively. Patients were grouped by age at diagnosis and the clinical parameters were compared between the groups.

Results: There were 102 females (89.5%) and 12 males (10.5%), with a female/male ratio of 8.5/1. The average age of the patients at diagnosis was 11.91±3.26 years. 77 (67.5%) patients have a positive family history. 14 (12.28%) patients have a concomitant autoimmune disease. On the first admission to the hospital, 47 (41.2%) patients were euthyroid, 46 (40.4%) patients were subclinical hypothyroid, 10 (8.8%) patients were overt hypothyroid, 3 (2.6%) patients were subclinical hyperthyroid, and 8 (7.0%) patients were overt hyperthyroid. Antithyroid peroxidase antibodies were positive in 109 (95.6%) and antithyroglobulin antibodies were positive in 105 (92.1%) of the patients. In the group under 12 years old, there were 7 (13.2%) patients with radiation exposure, whereas in the group over 12 years old, there was only 1 (1.9%) patient with radiation exposure, and thus the difference between the two groups was statistically meaningful.

Conclusion: Patients who have clinical and laboratory evidence of thyroid disease should be examined for autoimmune thyroiditis. Especially, it is very important that patients who have clinical evidence of other autoimmune diseases, have a family history of autoimmune thyroiditis, and/or a history of radiation exposure should be examined periodically and followed up closely.

Keywords: Autoimmune, children and adolescents, Hashimoto's thyroiditis.

Cite this article as: Arslan D, Yıldız FM, Kırmızıbekmez H. Clinical features in children and adolescents with Hashimoto's thyroiditis. Zeynep Kamil Med J 2024;55(2):67–70.

Received: October 23, 2023 **Revised:** November 14, 2023 **Accepted:** November 22, 2023 **Online:** May 06, 2024
Correspondence: Didar ARSLAN, MD. Uludağ Üniversitesi Tıp Fakültesi, Çocuk Yoğun Bakım Kliniği, Bursa, Türkiye.
Tel: +90 538 604 37 67 **e-mail:** didararslanbakan@hotmail.com
Zeynep Kamil Medical Journal published by Kare Publishing. Zeynep Kamil Tıp Dergisi, Kare Yayıncılık tarafından basılmıştır.

INTRODUCTION

Hashimoto's thyroiditis (chronic autoimmune thyroiditis) is the most common cause of goiter and acquired hypothyroidism among children and adolescents. It is characterized as an organ-specific autoimmune disorder in which both humoral and cellular immune responses play a role to varying degrees.[1–3] In childhood, Hashimoto's thyroiditis most commonly occurs in the early and intermediate periods of puberty.[4] The prevalence is four-seven times greater in females than in males.[5–7] Children and adolescents with Hashimoto's thyroiditis may be asymptomatic at the time of initial diagnosis, yet they may also present with symptoms associated with goiter and hypothyroidism.[8]

In a school-age child residing in an area not recognized for iodine deficiency, the presence of goiter, elevated TSH levels alongside normal T3 and T4 levels, and positive autoantibodies collectively indicate a likely diagnosis of Hashimoto's thyroiditis. Diagnosis is confirmed by the detection of high-titer autoantibodies in the blood.[1] In patients with Hashimoto's thyroiditis, the incidence of thyroid cancer is significantly higher than in the normal population.[9]

The present study investigates the demographic characteristics, clinical presentation features, and risk factors of patients diagnosed with Hashimoto's thyroiditis, along with any concurrent autoimmune disorders, and assesses the prevalence of thyroid nodules and their characteristics.

MATERIAL AND METHODS

The present study is based on a retrospective review of the medical charts of children and adolescents being followed up with a diagnosis of Hashimoto's thyroiditis in the Pediatric Endocrinology Outpatient Clinic of the Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center. Included in the study were 114 patients whose age, sex, presenting complaints, family history, radiation exposure history, presence of accompanying autoimmune or non-autoimmune conditions, presence of goiter on palpation, serum-free T4 (fT4) and thyroid-stimulating hormone (TSH) levels, anti-thyroid peroxidase antibody (anti-TPO), antithyroglobulin antibody (anti-Tg) levels, and thyroid ultrasound findings were reviewed retrospectively.

A positive family history was established when Hashimoto's thyroiditis was detected in the first- and second-degree relatives of the patient, and a history of severe systemic illness, trauma, and emotional stress were regarded as potential triggering factors. The study was approved by the ethics committee of Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center (17.10.2014; 168). The study was performed in compliance with the ethical standards of the 1964 Declaration of Helsinki.

Statistical Analysis

Descriptive statistics were analyzed using IBM SPSS Statistics (Version 22.0. Armonk, NY: IBM Corp.). A Chi-square test was used to compare categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Of the study patients, 102 (89.5%) were female and 12 (10.5%) were male, with a female-to-male ratio of 8.5:1. Of the total, 59 (51.8%) had been diagnosed during puberty and 55 (48.2%) before reaching puberty, with a mean age at the time of initial diagnosis of 11.91±3.26 years (3.5–17.5 years). While there were 54 patients (47.4%) before puberty (<12 years), there were 60 patients (52.6%) after puberty (>12 years).

Thyroid testing was prompted by various factors among the patients, including a neck lump in 23 individuals (20.7%), excessive weight concerns in 19 (17.1%), routine investigation subsequent to a diagnosis of type 1 diabetes mellitus in eight (7%), positive family history in six (5.3%), and short stature and growth retardation in five (4.5%) patients. The patients had most frequently sought medical attention at the outpatient clinic due to a neck lump complaint (20.7%), while the condition was incidentally discovered during investigations conducted for various other reasons in 10 patients (8.8%). A positive family history was identified in 77 (67.5%) patients, and eight patients (7%) had a history of radiation exposure for imaging purposes.

14 of 114 patients (12.28%) had an accompanying autoimmune disease. The most common accompanying autoimmune disease was type 1 DM (9 patients, 7.89%). One patient had Autoimmune Polyglandular Syndrome Type 2. Among the minor findings, vitiligo was present in 4 (3.5%) patients.

An evaluation of the thyroid examination findings from the time of the initial presentation revealed that 55 patients (48.2%) had a detectable goiter on palpation, including 51 (50%) of the male patients and four (33.3%) of the female patients. When the patients were assessed based on the results of thyroid function tests, 47 (41.2%) were identified as euthyroid at presentation, 46 (40.4%) had subclinical hypothyroidism, 10 (8.8%) had overt hypothyroidism, three (2.6%) had subclinical hyperthyroidism, and eight (7%) had overt hyperthyroidism.

Among the study patients, 105 (92.1%) showed positivity for antithyroglobulin (anti-Tg) antibodies, and 109 (95.6%) tested positive for anti-thyroid peroxidase (anti-TPO) antibodies, while 100 patients (87.7%) tested positive for both antibodies. Thyroid ultrasound (USG) findings at the time of initial diagnosis were available for 106 patients and revealed thyroid nodules in 22 patients (20.7%), in sizes ranging from 2.8 mm to 20 mm. During the follow-up of these patients, the thyroid nodules increased in size in four patients (18.1%), decreased in size in seven patients (31.8%), and completely disappeared in eight patients (36.3%). Over the course of follow-up, thyroid nodules showed no change in 91 patients (79.8%). Patients with thyroid nodules larger than 1 cm in size underwent fine needle aspiration biopsy, and the analysis of the specimens indicated benign lesions.

An analysis of the patients by age revealed no significant differences in variables such as family history, iodized salt consumption, presence of goiter, anti-TPO and anti-Tg positivity, presence of a nodule, TSH and fT4 levels, and nodule size between prepubertal and pubertal patients. Of the patients under the age of 12 years, seven (13.2%) had a history of radiation exposure, while only one patient (1.9%) above the age of 12 had such a history, and this difference was statistically significant (p<0.05). The distribution of risk factors across the age groups is presented in Table 1.

Table 1: Distribution of risk factors across age groups

Risk factor	≤12		>12		p
	n	%	n	%	
Positive family history	35	30.7	41	36	0.206
Radiation exposure	7	6.1	1	0.8	**0.027***
Iodized salt consumption	49	43	51	44.7	0.401
Triggering factor	12	10.5	13	11.4	0.861

Chi-square Test *: <0.05.

DISCUSSION

Hashimoto's thyroiditis (chronic lymphocytic thyroiditis) is the most common thyroid disorder observed in children and adolescents and is the leading cause of acquired hypothyroidism and goiter in areas not known to be endemic for iodine deficiency. While there are documented cases within the first three years of life, the condition most commonly occurs after the age of six years, and especially during early and mid-puberty.[1,4] The mean age at initial presentation in the present study was 11.9±3.2 years, concurring with the findings of similar studies conducted in Türkiye.[7,10–12] In our patient group, the female-to-male ratio was 8.5, which is higher than the ratios of 3.6 reported by Özsu et al.[10] and 5.7 reported by Özen et al.[13] in Türkiye.

The majority of patients with Hashimoto's thyroiditis present with an asymptomatically enlarged thyroid gland.[14] In the present study, 20.2% of the patients presented with a neck lump, while 17.6% presented with excessive weight. In the study by Demirbilek et al.,[7] a goiter was reported in 55% of the patients, 18.6% of whom exhibited clinical findings suggestive of hypothyroidism. Aside from goiter and neck discomfort, the most common symptoms that can be expected in patients with autoimmune thyroid disorders include fatigue, increased or decreased weight, sleep and attention disturbances, emotional changes, menstrual irregularities in females, and changes in bowel habits. These symptoms can vary based on whether the patient presents with hypothyroidism, euthyroidism, or hyperthyroidism at the time of diagnosis. In our study group, 64 of the patients (56.1%) presented with complaints that could be linked to thyroid disorders, while the remaining patients (43.9%) were identified incidentally during screening for other purposes or while undergoing testing for nonspecific findings.

It is advisable to conduct a more thorough search for clinical findings in patients with a family history of autoimmune thyroid disorders. First-degree relatives of patients with Hashimoto's thyroiditis often test positive for thyroid autoantibodies,[14] and supporting this finding from the literature, 67.5% of the patients in the present study had first- and second-degree relatives with a history of thyroid disorders.

Hashimoto's thyroiditis can occur alongside various other autoimmune disorders. Marinovic et al.[15] reported the presence of an additional autoimmune disorder in 17% of their patients with chronic autoimmune thyroiditis. Clinicians should remain vigilant for the presence of other autoimmune disorders in patients with an autoimmune condition. Clinical findings that are inconsistent with the current condition should raise suspicion of another autoimmune disorder, and the possibility of polyglandular syndrome should be considered. Antithyroid antibody positivity has been reported in 16–25% of children with type 1 diabetes mellitus.

In the present study, 12.2% of patients had an additional autoimmune disorder, while 7.89% of them had type 1 diabetes mellitus, and of these, 3.5% had vitiligo. Furthermore, one patient was diagnosed with autoimmune polyglandular syndrome type 2, determined based on the presence of adrenal insufficiency, autoimmune thyroiditis, celiac disease, diabetes, and autoantibody positivity.

The most significant difference between the two age groups in our study related to a history of radiation exposure, being more common among those diagnosed before the age of 12 than in the older age group. The thyroid gland is among the tissues most vulnerable to damage from radiation exposure. While there have been numerous studies to date commenting on the association between medical or environmental radiation exposure and thyroid malignancies, there is a lack of comprehensive knowledge of the other pathological processes that may occur in the thyroid gland.

Among the many studies exploring the long-term effects of environmental radiation exposure in the proximity of nuclear accident sites is a study of 1,441 children born during the Chernobyl accident, conducted when they were between the ages of 13 and 17 years. The study reported increased thyroid autoantibody positivity, but no increase in the prevalence of overt thyroid disorder.[16] A large-scale study of 100,000 trauma patients suggested that radiation exposure associated with computerized tomography scans could be justified considering the benefits provided by such imaging studies.[17] It has been well-established that most autoimmune disorders occurring in childhood are triggered by puberty.

The significant history of radiation exposure in the younger age group in our study suggests that it may accelerate the development of autoimmune disorders. The complex pathogenesis of thyroid autoimmunity may be triggered in susceptible cases, although such triggering is not necessarily dose-dependent.[18] Further research is required into the impact of radiation exposure on everyday life and during medical examinations of the thyroid gland.

Thyroid function tests conducted at the time of presentation reveal euthyroidism or hypothyroidism (overt or subclinical) in a significant proportion of patients with Hashimoto's thyroiditis, with hyperthyroidism being a rare occurrence in some cases.[19] In a study carried out by Özsu et al.,[10] euthyroidism was identified in 42.5% of the patients, subclinical hypothyroidism in 24.5%, overt hypothyroidism in 29.2%, and subclinical hyperthyroidism in 2.8%. In the present study, 41.2% of the patients had euthyroidism, 40.4% had subclinical hypothyroidism, 8.8% had overt hypothyroidism, 7% had hyperthyroidism, and 2.6% had subclinical hyperthyroidism, which is in concurrence with the findings of other studies conducted in Türkiye.

The greater prevalence of euthyroidism compared to overt hypothyroidism may be due to several factors, including early patient presentation, increased awareness in those with a family history of thyroid disorders, the regular inclusion of thyroid function tests in routine check-ups at many healthcare centers, and the increased accessibility to screening tests.

The incidence of thyroid cancers is higher in patients with lymphocytic thyroiditis than in the general population. The form of thyroid cancer that most commonly occurs in association with lymphocytic thyroiditis is papillary thyroid carcinoma.[20] In a study conducted in Türkiye, one case of papillary thyroid carcinoma was reported among 162 children and adolescents with Hashimoto's thyroiditis.[7] As our study sample comprised young patients with a relatively short disease duration, there was only one patient who necessitated further investigation for thyroid carcinoma, and no other patients required such examination.

CONCLUSION

The large number of patients diagnosed before the age of 12 in the present study suggests that autoimmune disorders should not be overlooked in young children. The greater incidence of radiation exposure in the younger age group may indicate that environmental influences can shift the onset of the disease to earlier ages in those who are susceptible to autoimmunity. Since the present study involves a two-year follow-up of patients after diagnosis, the results do not reflect the long-term consequences. Lifelong follow-up is essential for patients diagnosed at a young age and for those in high-risk groups.

The findings of the present study also emphasize the need to keep other factors in mind, such as the presence of concurrent autoimmune conditions, a family history of autoimmune thyroid disease, and the incidental detection of elevated TSH levels.

Statement

Ethics Committee Approval: The Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center Clinical Research Ethics Committee granted approval for this study (date: 17.10.2014, number: 168).

Author Contributions: Concept – FMY; Design – FMY, DA; Supervision – HK, FMY; Resource – HK; Materials – HK, DA; Data Collection and/or Processing – HK, DA; Analysis and/or Interpretation – HK, DA; Literature Search – DA; Writing – DA, HK; Critical Reviews – FMY.

Conflict of Interest: The authors have no conflict of interest to declare.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

REFERENCES

1. LaFranchi S. Disorders of the Thyroid Gland; Chapter 567 Thyroiditis. In: Behrman RE, Jensen HB, Stanson BF, Kliegman RM, editors. Nelson Textbook of Pediatrics. 18. Philadelphia: WB Saunders; 2007. p.2327–9.
2. Fisher DA, Grueters A. Thyroid disorders in childhood and adolescents. In: Sperling MA, editor. Pediatric endocrinology. 3rd ed. Amsterdam: Elsevier; 2008. p.236–8.
3. Weetman AP, McGregor AM. Autoimmune thyroid disease: Further developments in our understanding. Endocr Rev 1994;15:788–830.
4. Gönç EN, Yordam N. Çocukluk ve adölesanda tiroid hastalıkları. In: Öcal G, Nurşen Y, Kurtoğlu S Günöz H, editorler. Pediatrik endokrinoloji. 1. baskı. Ankara: Kalkan Matbacalık; 2003. p.261–70.
5. Rallison ML, Dobyns BM, Meikle AW, Bishop M, Lyon JL, Stevens W. Natural history of thyroid abnormalities: Prevalence, incidence, and regression of thyroid diseases in adolescents and young adults. Am J Med 1991;91:363–70.
6. Desai MP, Karandikar S. Autoimmune thyroid disease in childhood: A study of children and their families. Indian Pediatr 1999;36:659–68.
7. Demirbilek H. Çocuk ve adölesanlarda Hashimoto tiroiditinin klinik özellikleri, tedavisi ve prognozunun incelenmesi. Tıpta Uzmanlık Tezi. Ankara: Hacettepe Üniversitesi Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları Anabilim Dalı; 2004.
8. de Vries L, Bulvik S, Phillip M. Chronic autoimmune thyroiditis in children and adolescents: At presentation and during long-term follow-up. Arch Dis Child 2009;94:33–7.
9. Intidhar Labidi S, Chaabouni AM, Kraiem T, Attia N, Gritli S, El May A, et al. Thyroid carcinoma and Hashimoto thyroiditis. Ann Otolaryngol Chir Cervicofac [Article in French] 2006;123:175–8.
10. Özsu E, Yeşiltepe Mutlu RG, Çizmeci F, Hatun Ş. Hashimoto tiroiditli hastalarımızın özellikleri. Türk Ped Arş 2011;46:252–5.
11. Yavuz K, Aylanç H. Retrospective evaluation of clinical and laboratory features of pediatric patients with Hashimoto's thyroiditis. Troia Med J [Article in Turkish] 2021;2:85–9.
12. Yeşilkaya E, Belen B, Bideci A, Çamurdan O, Boyraz M, Cinaz P. Kronik otoimmün tiroiditli çocuk ve ergenlerin klinik özellikleri. Gülhane Tıp Derg 2008;50:147–50.
13. Özen S, Berk Ö, Şimşek DG, Darcan S. Clinical course of Hashimoto's thyroiditis and effects of levothyroxine therapy on the clinical course of the disease in children and adolescents. J Clin Res Pediatr Endocrinol 2011;3:192–7.
14. Dallas JS, Foley TP. Thyromegaly. In: Lifshitz F, editor. Pediatric endocrinology. 4th ed. New York: Marcel Dekker; 2003. p.393–406.
15. Marinovic D, Léger J, Garel C, Czernichow P. Chronic autoimmune thyroiditis in the child. Arch Pediatr [Article in French] 2000;7:1284–92.
16. Agate L, Mariotti S, Elisei R, Mossa P, Pacini F, Molinaro E, et al. Thyroid autoantibodies and thyroid function in subjects exposed to Chernobyl fallout during childhood: Evidence for a transient radiation-induced elevation of serum thyroid antibodies without an increase in thyroid autoimmune disease. J Clin Endocrinol Metab 2008;93:2729–36.
17. Hikino K, Yamamoto LG. The benefit of neck computed tomography compared with its harm (risk of cancer). J Trauma Acute Care Surg 2015;78:126–31.
18. Eheman CR, Garbe P, Tuttle RM. Autoimmune thyroid disease associated with environmental thyroidal irradiation. Thyroid 2003;13:453–64.
19. Demirbilek H, Kandemir N, Gonc EN, Ozon A, Alikasifoglu A, Yordam N. Hashimoto's thyroiditis in children and adolescents: A retrospective study on clinical, epidemiological and laboratory properties of the disease. J Pediatr Endocrinol Metab 2007;20:1199–205.
20. Ersoy R, Gül K, Korukçuoğlu B, Ersoy P, Aydın R, Aydın C, et al. Coexisting thyroid papillary carcinoma with chronic lymphocytic thyroidits. Turkish Med J [Article in Turkish] 2007;1:119–22.