

# Incidence of thyroid nodules in children affected by Hashimoto's Thyroiditis: a twelve year survey of 793 children

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## Introduction

Hashimoto's Thyroiditis (HT) has been linked to papillary cancer in adults but not in children and adolescents. Moreover, there is no agreement on the more appropriate frequency of thyroid ultrasound (US) in the follow-up of children with HT. The overall incidence of thyroid cancer among childhood thyroid nodules has been reported to be 26.4% in a review by Niedziela. However, the prevalence of nodular disease and thyroid cancer among pediatric patients with autoimmune thyroiditis is not known. Data from a study published by Corrias et al in 2008 showed that thyroid nodular disease is present in 31.5% of pediatric patients with HT and that cancer occurs in at least 9.6% of cases.

## Objectives

- To investigate the incidence of thyroid nodules and of thyroid cancer in a large group of children and adolescents (793) with HT followed-up for a mean period of 4.4 years (1.2 to 12.8 years)
- To look for possible predictive factors for the development of thyroid nodules

## Methods

**Patients:** We evaluated 793 (176 m, 617 f, mean age at diagnosis  $10.7 \pm 2.9$  y) children and adolescents with HT attending 8 Italian Centres of Paediatric Endocrinology. Data were retrospectively collected from the clinical notes, during the period between 2002- 2014.

HT was diagnosed on the basis of typical ultrasound imaging (US) and presence of thyroid peroxidase (TPOab) and/or thyroglobulin (TGab) antibodies.

Fifteen patients had also Turner's syndrome, 9 Down's syndrome, 1 Klinefelter's syndrome, 31 vitiligo, 52 coeliac disease, 12 insulin-dependent diabetes mellitus, 22 alopecia, 2 Addison's disease and 198 presented with goiter. A positive family history for autoimmune diseases was present in 323 (40,7%) of the patients.

**Study protocol:** At each visit the auxological data were recorded, TSH, fT4, TPO- and TG-antibodies were measured and a US was performed to assess the thyroid volume, detect nodules > 0.5 mm and to classify the echographic changes (score 1 to 5). The presence of lymphadenopathy or palpable nodules, treatment with L thyroxine, results of eventual fine needle biopsy (FNB) were also recorded.

## Results: time of diagnosis

The median period of follow-up was for 4.4 years (1.2 to 12.8 years). At the time of diagnosis, mean TSH was  $19.5 \pm 77.9$   $\mu$ U/ml (range 0-1000; nv 0.3-3.69), and fT4 was  $8.5 \pm 6.1$  pg/ml (range 0.46-67.4; nv 9-17.7). US examination revealed that 65 patients (8.2%) had nodules with a diameter >5 mm, and 145 patients had a thyroid volume >+2 SD. Ten FNB were performed based on US findings.

Three patients (2 F and 1 M) had a concomitant thyroid cancer (papillary carcinoma). Two of them showed lymphadenopathy, and two had a single nodule.

## Results: follow-up

The incidence of nodules was 3.5% per year with a cumulative number of 152 (19,2%) cases at the end of the follow-up. Only a thyroid score of more than 2 (severe parcelled hypoechogenicity) was predictive for the appearance of new nodules. No correlation was found with the levels of TSH. Papillary cancer was found in two females and two males. The frequency of cancer among patients with nodules was 4,6%.

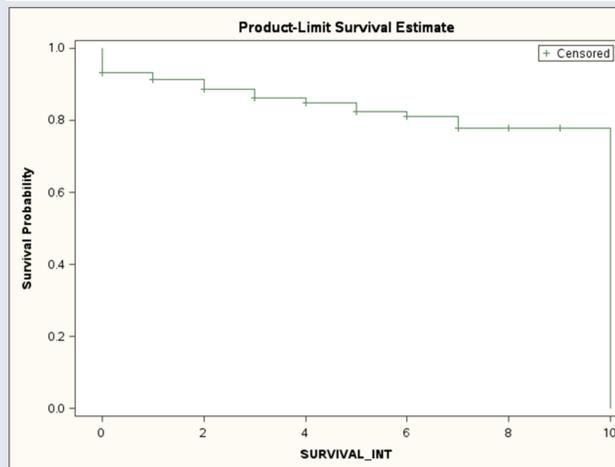


Fig.1:  
A 10 years' population survival curve without thyroid nodules

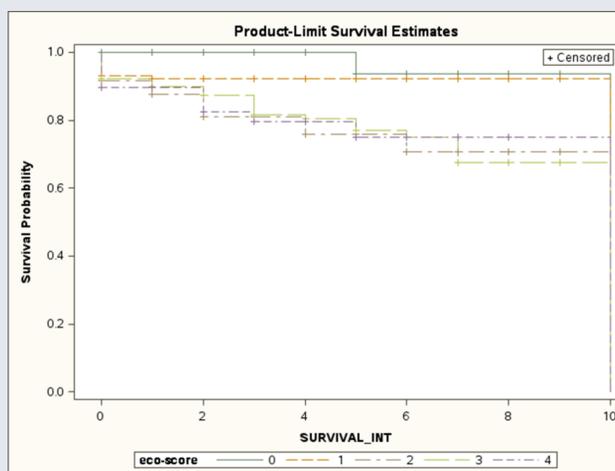


Fig.2:  
Reduced survival curve for population with thyroid score greater than 2.  
p-value: 0,0044

Table 1: Features of patientes who developed a thyroid cancer

	Patient 1	Patient 2	Patient 3	Patient 4
Sex and age	Female; 11,7	Female; 12,2	Male; 12,8	Male; 12
Palpable nodule			yes	
Lympho-adenopathy		yes	yes	yes
Number of nodules	2	1	1	>2
Nodule present at time of diagnosis	yes		yes	
Years since HT diagnosis	3,7	4,6	1,1	4,1
Histological diagnosis	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma	Papillary carcinoma

## Conclusions

- **The inflammatory state of the thyroid gland, evaluated by US, is a predictive factor for the development of thyroid nodules.**
- **No correlation was found between the incidence of nodules and the levels of TSH.**
- **Since a thyroid nodule is the typical presentation of thyroid cancer, we suggest that patients with a high inflammatory state of the gland be more closely monitored.**
- **Thyroid nodules in paediatric patients with HT are less often malignant than solitary nodules (4,6% vs 26%;p<0.0001).**

## References

1. Corrias A, Cassio A, Weber G, et al. Thyroid nodules and cancer in children and adolescents affected by autoimmune thyroiditis. Archives of pediatrics & adolescent medicine 2008;162:526-31.
2. Niedziela M. Pathogenesis, diagnosis and management of thyroid nodules in children. Endocrine-related cancer 2006;13:427-53.