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Original Article

Subclinical Hypothyroidism in Children: Natural History, Risk Factors, and Outcomes

Nur Şeyma Zengin[1], Elif Sağsak[2], Seda Geylani Güleç[1]
[1]University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital, Clinic of Pediatrics, İstanbul, Türkiye
[2]University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital, Clinic of Pediatric Endocrinology, İstanbul, Türkiye

What is already known on this topic?
-Subclinical hypothyroidism (SH) in children is a relatively uncommon but increasingly recognized condition, with variable natural history.
-Most cases are idiopathic and often show spontaneous resolution or stable course without progression.

What this study adds?
-This study provides one of the largest pediatric cohorts with mild subclinical hypothyroidism (SH) in Turkey, demonstrating its predominantly benign course.
-Higher baseline thyroid-stimulating hormone (TSH) levels and Hashimoto's thyroiditis emerge as key factors associated with progression.
-Stable growth parameters across follow-up support that untreated mild SH does not adversely affect growth.

Abstract
Background: Subclinical hypothyroidism (SH) is defined by elevated thyroid-stimulating hormone (TSH) with normal thyroid hormone levels and typically presents without specific symptoms in children. Although treatment criteria exist, predictors of progression and treatment need remain uncertain.
Objective: To evaluate the natural course of mild SH, identify clinical conditions associated with elevated TSH, determine predictors of progression requiring levothyroxine, and assess growth outcomes.
Methods: Records of 111 children (3 months–18 years) with mild SH (TSH 5–10 mIU/L on ≥ 2 measurements) and ≥ 6 months of follow-up were retrospectively reviewed. Demographic, biochemical, anthropometric, etiological, and imaging data were analyzed. Children were categorized as idiopathic or as having associated clinical factors (autoimmune thyroiditis, iodine imbalance, obesity, or medication use). Outcomes were classified as euthyroid, persistent SH, or requiring treatment.
Results: During follow-up, 45 children (40.5%) became euthyroid, 49 (44.2%) remained subclinically hypothyroid, and 17 (15.3%) required levothyroxine. Idiopathic cases showed the most favorable course, with only 8.6% requiring therapy. Hashimoto's thyroiditis (HT) was the strongest predictor of progression (42.1% vs. 9.8% in non-HT). A baseline TSH > 7.5 mIU/L increased treatment likelihood by ~3.5-fold. Growth parameters remained within normal limits, with no deterioration in untreated children.
Conclusions: Mild pediatric SH is generally benign and self-limited, particularly in idiopathic cases. HT and higher baseline TSH levels are key predictors of progression, while growth remains stable. Management should be individualized based on underlying conditions, TSH severity, and autoimmune status.
Keywords: Natural history, risk factors, subclinical hypothyroidism

Nur Şeyma Zengin, MD,
University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital, Clinic of Pediatrics, İstanbul, Türkiye
nszengin37@hotmail.com
https://orcid.org/0000-0001-7926-0064

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Introduction

Subclinical hypothyroidism (SH) is defined by elevated serum thyroid-stimulating hormone (TSH) with normal thyroid hormone levels and the absence of specific clinical signs (1, 2). The normal range of TSH (approximately 0.4–0.5 to 4.0–5.0 μIU/mL) varies across assays, and mild SH, typically defined as TSH 4.5–10 mIU/L, represents most pediatric cases (3, 4). Several descriptive terms are used in clinical practice to characterize mild TSH elevation. "Isolated hyperthyrotropinemia" refers to mild or transient increases in TSH levels without evidence of intrinsic thyroid dysfunction, whereas "primary compensated hypothyroidism" denotes early thyroid impairment that warrants closer clinical observation. Importantly, mild TSH elevation does not always indicate true thyroid disease; transient increases associated with obesity, fluctuations in iodine intake, or recovery from non-thyroidal illness may represent adaptive physiological responses rather than pathological conditions (5).
In children, SH arises in a wide range of clinical contexts, including autoimmune thyroiditis, iodine imbalance, congenital thyroid anomalies, genetic syndromes, medication effects, and idiopathic presentations (6, 7).
Idiopathic SH is characterized by mildly elevated TSH levels despite normal peripheral thyroid hormones and the absence of autoimmunity or identifiable secondary contributors (3). Most children are asymptomatic; occasional nonspecific symptoms such as dry skin, fatigue, or weight gain are not diagnostic(8-10).
The natural history of SH differs between children and adults. Pediatric SH often remains stable or normalizes spontaneously, and progression to overt hypothyroidism (OH) occurs in a minority of cases (0–28%) (11-13).
Children with SH due to HT have a higher risk of deterioration (14, 15), a risk that may further increase in chromosomal disorders such as Turner or Down syndrome (13). Among clinical and biochemical variables, baseline TSH is considered the strongest predictor of outcome (16).
Although OH impairs growth and neurocognitive development, the significance of untreated mild SH remains uncertain. Most evidence indicates no adverse effects on growth, bone maturation, or cognition, though subtle metabolic changes have been described (2, 4).

Current recommendations favor observation in asymptomatic, antibody-negative children with TSH <10 mIU/L, and treatment in those with symptoms, goiter, autoimmunity, or rising TSH (4, 10, 17, 18).
Given these considerations, this study aimed to characterize the natural course of mild SH, identify clinical conditions that accompany TSH elevation and may provide a background for SH, determine predictors of progression requiring treatment, and evaluate growth outcomes in affected children.

Materials and methods

Study Design and Population

This single-center retrospective study included children aged 3 months to 18 years who presented to the pediatric endocrinology outpatient clinic of Gaziosmanpaşa Training and Research Hospital between 2016 and 2019. Among 175 patients initially identified with mildly elevated TSH, 111 were eligible after excluding those with follow-up < 6 months or loss to follow-up. None had received thyroid-related treatment at admission.
Mild (SH) was defined as two TSH measurements of 5–10 mIU/L obtained ≥4 weeks apart, with normal free thyroxine (fT4) levels. Since SH is a biochemical state, conditions potentially influencing TSH (e.g., obesity, genetic syndromes, medication use, prior chemotherapy/radiotherapy) were not exclusion criteria. Patients with TSH > 10 mIU/L, abnormal fT4, or known thyroid disease requiring treatment were excluded.

Study Procedure

The following variables were collected: date of admission, sex, presenting symptoms, age, history of regular medication use, comorbidities, use of iodized salt, family history of thyroid disease, height, body weight, physical examination findings, TSH, fT4, free triiodothyronine (fT3), anti-thyroid peroxidase (anti-TPO), anti-thyroglobulin (anti-Tg), urinary iodine concentration, and thyroid ultrasonography (USG) results. These variables were used to evaluate potential factors associated with mild SH, risk factors for requiring treatment, growth outcomes, and indications for therapy.
The etiological classification was made based on potential contributing factors described in the pediatric endocrinology literature; no causality was inferred. Conditions such as autoimmune thyroiditis, obesity, genetic syndromes, iodine deficiency, congenital thyroid malformations, medications affecting thyroid function, and history of radiotherapy or chemotherapy were examined.
For growth evaluation, height, weight, Body Mass Index (BMI), and growth velocity were expressed as Standard Deviation Score (SDS) using Neyzi's references (19). Growth velocity SDS was calculated using Neyzi's charts for girls aged 8–13 and boys aged 10–15, and Baumgartner's data for younger ages (20). Growth velocity could not be assessed in 37 patients due to levothyroxine initiation, epiphyseal closure, growth-affecting medications, Down syndrome, or prior chemotherapy.
Serum TSH, fT4, and fT3 were measured with immunoenzymatic assays on Beckman Coulter DXI 800 analyzers. Anti-TPO > 9 IU/mL and anti-Tg > 4 IU/mL were considered positive.
Urinary Iodine Concentration (UIC) was analyzed externally (Düzen Laboratory, Turkey) using an ICP-MS system. Reference intervals were based on the World Health Organization (WHO) 2007 guideline, originally expressed in µg/L (21). After unit conversion, these correspond to the standard µg/L categories. UIC levels were therefore classified according to WHO 2007 criteria (21): < 20 µg/L severe; 20–49 µg/L moderate; 50–99 µg/L mild; 100–199 µg/L adequate; 200–299 µg/L above requirements; ≥300 µg/L excessive.

Patient follow-up and treatment

After the diagnosis of SH (defined as elevated TSH and normal fT4 levels on at least two separate measurements) was confirmed, the date of diagnosis was designated as "Day 0." Following this, risk factors associated with the need for treatment, including autoimmune thyroiditis, goiter, higher baseline TSH levels, obesity, and chromosomal or autoimmune comorbidities such as Turner syndrome, were evaluated. In patients with goiter or strong risk indicators, thyroid ultrasonography was performed to assess gland size and echogenicity heterogeneity suggestive of autoimmune thyroiditis.
In routine practice, patients without risk factors were advised to undergo clinical evaluation and TSH/fT4 measurement every 3–6 months, whereas those with goiter, autoimmune thyroiditis, higher baseline TSH levels (> 7.5–10 mIU/L), or other high-risk features were scheduled for re-evaluation within 1–3 months. However, due to the retrospective design of the study, variable appointment adherence, and differences in healthcare accessibility, follow-up intervals varied among patients. Therefore, only the initial (diagnostic) and the last available follow-up visits were included in the analysis, and patients with a follow-up duration of less than six months were excluded. The decision to initiate levothyroxine therapy was based on predefined biochemical and clinical indicators consistent with standard clinical practice. Specifically, TSH levels >10 mIU/L, a decline or downward trend in fT4, the presence of goiter, or clinical signs suggestive of OH were accepted as primary criteria for treatment initiation.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro–Wilk test. Descriptive statistics (mean, standard deviation, frequency) were calculated. Group comparisons for normally distributed variables were performed using the Student's t-test for two groups and one-way ANOVA for more than two groups; differences between baseline and follow-up values were evaluated with the paired-samples t-test. Correlations between normally distributed parameters were assessed using Pearson correlation coefficients. The mean growth velocity SDS was compared with population reference values for healthy children using the one-sample t-test. Categorical variables were analyzed using the Pearson chi-square test or Fisher's exact test, and the Fisher–Freeman–Halton test was applied for larger contingency tables. The linear-by-linear association test was used to assess trends across ordered categories. To estimate the association between baseline TSH levels and treatment requirement, the odds ratio (95% confidence interval) was calculated. A p-value < 0.05 was considered statistically significant.

Ethical Approval

This study was conducted as a specialty thesis in the Department of Pediatrics, Gaziosmanpaşa Training and Research Hospital. The study was carried out in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Taksim Training and Research Hospital (Date: 24.07.2019, Approval No: 102). Due to the retrospective design of the study, informed consent was not required.

Results

General Characteristics of the Patients

A total of 111 children with mild SH were included (Table 1). A family history of thyroid disease was present in 49 patients (44.1%), most commonly thyroid nodules (46.9%), goiter (20.4%), autoimmune thyroiditis (12.2%), hypothyroidism (8.2%), thyroid cancer (2.0%), and unspecified thyroid disorders (10.2%).

Overall follow-up outcomes

During follow-up, 45 children (40.5%) became euthyroid, 49 (44.2%) remained subclinically hypothyroid, and 17 (15.3%) required levothyroxine. Of those requiring treatment, 10 (58.8%) were female and 7 (41.2%) were male.
Treatment indications were TSH >10 mIU/L alone (n = 7; 41.2%), low fT4 (n = 3; 17.6%), newly developed goiter (n = 3; 17.6%), goiter accompanied by TSH >10 mIU/L (n = 1; 5.9%), short stature (n = 2; 11.8%), and weight loss with poor appetite (n = 1; 5.9%) (Figure 1). Among treated children, 1 had valproic acid use (TSH>10 mIU/L) and 1 had prior chemotherapy/radiotherapy (low fT4). Overall, 58.8% were treated due to biochemical deterioration, 35.3% due to clinical or structural findings, and 5.9% due to combined abnormalities.

Children requiring treatment had higher baseline TSH levels (p = 0.012). Baseline TSH levels differed significantly among follow-up outcome groups (Kruskal–Wallis test, p = 0.018), with post-hoc analyses demonstrating that this difference was primarily driven by higher baseline TSH levels in children who required treatment compared with those who became euthyroid (adjusted p = 0.020). Although children requiring treatment tended to be older at diagnosis (p = 0.049), post-hoc analyses did not confirm a statistically significant age difference between groups. Sex distribution, family history, BMI SDS, and urinary iodine status did not differ significantly. Detailed baseline comparisons according to follow-up outcomes are provided in Table 2.

Potential factors contributing to the etiology of subclinical hypothyroidism

Among the 111 children with SH, no specific etiological factor was identified in 70 patients (63%). Factors contributing to the etiology included autoimmune thyroiditis (HT; n = 19, 17.1%), low urinary iodine concentrations (n = 10; 9%), obesity (n = 9; 8.1%), valproic acid use (n = 5; 4.5%), and Down syndrome (n = 4; 3.6%). Additionally, one patient (0.9%) had a history of radiotherapy/chemotherapy, and one (0.9%) had congenital agenesis of the right thyroid lobe. Several children had overlapping factors, including HT with iodine deficiency (n = 2), HT with valproic acid therapy (n = 1), HT with obesity (n = 3), and Down syndrome with valproic acid therapy (n = 1). Therefore, the total number of etiology-contributing factors (n = 119) exceeded the number of patients.

Comparison according to the presence of Hashimoto's thyroiditis

A total of 19 patients (17.1%) had HT, while 92 (82.9%) had no autoimmunity. Patients with HT were older at both baseline and final visits (p < 0.001 for both), and female predominance was more pronounced (78.9% vs. 52.2%, p = 0.013). Baseline TSH and follow-up duration were similar between groups (p = 0.681 and p = 0.853).

At follow-up, euthyroidism was achieved in 26.3% of HT patients and 43.5% of non-HT patients (p = 0.048), while persistence of SH was comparable (31.6% vs. 46.7%, p = 0.484). Levothyroxine therapy was required significantly more often in the HT group (42.1% vs. 9.8%, p = 0.005) (Table3). Consistently, HT was more frequent in the treatment group (47.1%) than in the euthyroid (11.1%) or persistent SH groups (12.2%) (p = 0.005) (Table 2).

Among treated patients, indications differed by HT status. In the HT group (n = 8), treatment was initiated for goiter (n = 3), TSH > 10 mIU/L (n = 2), low fT4 (n = 2), or combined goiter + elevated TSH (n = 1). In the non-HT group (n = 9), indications included TSH > 10 mIU/L (n = 5), low fT4 (n = 1), short stature (n = 2), and weight loss with poor appetite (n = 1) (Table 3).

To isolate autoimmune effects, patients with HT plus additional etiological factors were excluded. Among isolated HT cases (n = 13), 30.8% became euthyroid, 38.5% remained subclinically hypothyroid, and 30.8% required treatment. In idiopathic SH (n = 70), these rates were 45.7%, 45.7%, and 8.6%, respectively (p = 0.075).

Urinary iodine status

Urinary iodine was measured in 39 patients: severe deficiency in 1 (2.6%), moderate in 1 (2.6%), mild in 8 (20.5%), optimal levels in 18 (46.2%), levels indicating risk for iodine-induced hyperthyroidism in 5 (12.8%), and other adverse outcomes in 6 (15.4%) (Table 2).

Baseline TSH and Treatment Requirement

When patients were categorized by baseline TSH level, those with TSH > 7.5 mIU/L had a significantly higher likelihood of requiring levothyroxine therapy compared with those whose baseline TSH was ≤ 7.5 mIU/L (27.0% vs. 9.5%). This association remained significant in both Pearson's chi-square (p = 0.015) and Fisher's exact test (p = 0.024), and was further supported by the likelihood ratio test (p = 0.019) and a significant linear-by-linear trend (p = 0.016). Children with baseline TSH > 7.5 mIU/L had approximately 3.5-fold higher odds of treatment initiation (OR = 3.55; 95% CI: 1.22–10.28) (Table 4).

Changes in Thyroid Hormone Levels

TSH levels declined significantly from baseline to final visit (p < 0.001), while fT4 remained stable (p = 0.605).

TSH Changes by BMI-SDS Classification

Of 111 children, 8.1% were obese (n = 9), 18.9% overweight (n = 21), 71.2% normal weight (n = 79), and 1.8% underweight (n = 2). Baseline TSH did not differ between groups (p = 0.614).

At the final visit, TSH differed significantly among BMI categories (p = 0.012). Obese children had higher final TSH than normal-weight (p = 0.036) and overweight peers (p = 0.007). No difference was found between normal-weight and overweight groups (p = 0.479).

During follow-up, TSH decreased significantly in normal-weight and overweight groups (both p < 0.001), but not in obese (p = 0.648) or underweight children (p = 0.727) (Table 5). TSH normalization was more frequent in non-obese children.

Clinical Outcomes by BMI-SDS

In the outcome evaluation according to BMI-SDS groups, among 111 children with SH, progression requiring levothyroxine therapy was observed in 12 of 79 normal-weight children (15.2%), 2 of 21 overweight children (9.5%), and 3 of 9 obese children (33.3%). However, the difference among groups was not statistically significant (p = 0.282).

Growth Outcomes

No significant changes in weight SDS, height SDS, or BMI SDS were observed between baseline and follow-up (all p > 0.05). Among untreated children (n = 94), baseline and final anthropometric values were also similar.

Growth velocity in untreated patients (n = 74) remained normal (mean SDS = 0.21±1.32; median = 0.16; p = 0.172).

Discussion

Our findings contribute to the limited evidence on the natural course and determinants of SH in childhood. Previous studies have reported a pediatric SH prevalence ranging from 1% to 9.5% (3, 22, 23). The widespread use of thyroid testing in routine pediatric care has increased incidental detections, creating uncertainty about which children require treatment and which can be safely monitored.

In this cohort, most children with mild SH either normalized or maintained stable thyroid function during follow-up. Only 15.3% eventually required levothyroxine therapy. When the analysis was restricted to the idiopathic subgroup, the treatment requirement decreased to 8.6%. This supports the concept that SH without identifiable pathology usually follows a benign course (22, 24).

These observations agree with the findings of De Luca et al., who showed decreasing TSH levels, stable fT4 levels, and no adverse clinical outcomes in children with idiopathic SH followed for two years (25). Taken together, these results support a conservative management approach unless biochemical or clinical deterioration occurs.

In our study, levothyroxine was initiated for markedly elevated TSH, low fT4, the development of goiter, or other clinically relevant findings, including short stature or weight loss with poor appetite, when judged to be potentially related to thyroid dysfunction. Only 11 of 111 children (9.9%) required treatment solely due to biochemical deterioration, which aligns with reports indicating that mild pediatric SH rarely requires therapy in the absence of autoimmunity or structural abnormalities (26). In the literature, the proportion of children with mild SH requiring medical treatment has been reported to range between approximately 2% and 12% (22, 27). Our findings indicate that the natural course of SH varies according to the underlying etiology.

The etiological background of SH in childhood is diverse. In our cohort, no specific etiology was identified in 63 percent of patients, consistent with previous reports in which idiopathic cases constitute the majority (28). In the remaining patients, factors thought to predispose to SH included HT, iodine imbalance, obesity, and medication-related effects.

HT was the most common identifiable cause in our cohort (17.1%). It predominantly affected older and female patients, consistent with reported epidemiology (29-31). The clinical course was less favorable in children with HT. Treatment was required in 42.1% of children with HT compared with 9.8% of those without autoimmunity. Even when the comparison was restricted to isolated HT and idiopathic SH,

progression remained more frequent in the HT group (30.8% vs. 8.6%). These findings align with multicenter studies reporting a higher risk of progression when SH coexists with thyroid autoimmunity (13, 32-34). In HT positive children, goiter or biochemical decline were major determinants of treatment. In idiopathic SH, treatment was mainly initiated for rising TSH or growth related concerns. This pattern suggests that idiopathic SH generally follows a stable course, whereas in HT-positive children treatment decisions were more often driven by objective findings such as goiter or biochemical deterioration.

Iodine status is an important component of thyroid physiology (35-38). Although some population studies have described a U shaped association betweenUIC and TSH (39), a recent meta analysis found inconsistent relationships in the mild to moderate deficiency range (40). In our cohort, severe iodine deficiency was uncommon, whereas mild to moderate deficiency was more frequent. Because UIC was measured only once and in a relatively limited subset of patients, these findings should be interpreted with caution, as single measurements may reflect short-term dietary fluctuations rather than true, persistent deficiency. All children with iodine deficiency were advised to use iodized salt; however, only one patient with documented deficiency reported not consuming iodized salt. As UIC was not reassessed during follow-up, the effect of iodine supplementation on subsequent TSH trajectories could not be evaluated, representing an inherent limitation of the retrospective study design.

Obesity has been associated with higher TSH levels in numerous pediatric studies. The prevalence of SH ranges between 7–23% in obese children, whereas it remains around 2% in their normal-weight peers (41, 42), and national data from the KNHANES VI similarly reported SH rates of 24.3% in obese and 12.8% in non-obese children (43). In our cohort, 27.9% of children were overweight or obese, which is consistent with previous reports (27, 44). Although the mechanism underlying elevated TSH in obesity is not fully understood, increased leptin is known to stimulate Thyrotropin Releasing Hormone (TRH) and TSH secretion, while weight loss reduces both leptin and TSH levels (45, 46). In our cohort, baseline TSH levels did not differ significantly across BMI groups; however, during follow-up, TSH elevation persisted in obese children, whereas significant declines were observed in normal-weight and overweight peers. Although treatment was required more frequently in obese children, this difference did not reach statistical significance. These findings suggest that TSH elevation in obesity may reflect not only an adaptive response but, in some cases, early alterations in the hypothalamic–pituitary–thyroid axis (46-49).

The magnitude of TSH elevation at diagnosis serves as a surrogate for the intrinsic functional reserve of the thyroid axis. Although pediatric SH generally follows a benign and often reversible course, our findings highlight that children with baseline TSH greater than 7.5 mIU/L constitute a subgroup with a higher likelihood of deterioration. Recognizing this threshold may assist clinicians in identifying patients who require closer follow-up and earlier therapeutic consideration.

Growth and bone development were not adversely affected in our cohort, consistent with several previous studies. Longitudinal studies in untreated children with SH have similarly reported no significant changes in height SDS, BMI SDS, or growth velocity compared with healthy controls, suggesting that mild thyroid dysfunction does not interfere with growth regulation (12, 24, 27, 50).

In our cohort, mean growth velocity SDS was 0.21 ± 1.32, which was comparable to the population mean, further supporting that mild SH is unlikely to impair somatic growth or bone maturation in the short to medium term.

Overall, our study supports the growing body of evidence that idiopathic pediatric SH is often a benign and self-limiting condition, whereas SH associated with Hashimoto's thyroiditis carries a higher likelihood of requiring treatment. Baseline TSH > 7.5 mIU/L also appears to be a predictive factor. Management decisions should be individualized, taking into account the underlying etiology, the severity of biochemical abnormalities, and the presence of clinical features.

Study Limitations

This study has several limitations. First, its retrospective design resulted in heterogeneous follow-up intervals and variable follow-up durations, which may have influenced the estimation of progression or regression rates. Second, the overall follow-up period was relatively short, limiting the ability to fully characterize the long-term natural course of mild SH and its potential effects on growth. Future prospective studies with standardized and extended follow-up schedules are warranted.

A small number of patients presented with clinical factors known to influence TSH levels such as genetic syndromes (e.g., Down syndrome), use of medications affecting thyroid function (e.g., valproic acid), or a history of chemotherapy/radiotherapy. These cases were intentionally included to reflect real-world clinical practice; however, they may introduce potential confounding and should be considered when interpreting the results.

Finally, although predefined index and final visits were used to minimize bias arising from irregular appointment intervals, this approach while improving generalizability limits the evaluation of time-dependent trends in thyroid function.

Conclusion

In this cohort, mild SH in children demonstrated a predominantly benign and stable course. Idiopathic cases showed the most favorable outcomes, whereas HT and higher baseline TSH levels were the main predictors of progression requiring treatment. Although TSH elevations tended to persist in obese children, no adverse effects on growth were observed. These findings support an individualized follow-up strategy based on underlying clinical conditions, baseline TSH severity, and autoimmune status. Larger prospective studies are needed to refine risk-based monitoring and management approaches.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Table 1. General Characteristics of the Patients

Variable	Mean ± SD	Min–Max	n	%
Age (years)			111	
First visit	8.28 ± 4.39	0.37–17.0		
Last visit	9.14 ± 4.47	1.0–17.6		
Follow-up duration (years)	0.86 ± 0.53	0.5–3.0	111	
Gender			111	
Female			59	53.2
Male			52	46.8
Family history of thyroid disease			111	
Absent			62	55.9
Present			49	44.1
Body weight SDS			111	
First visit	–0.06 ± 1.31	–3.50–2.96		
Last visit	–0.09 ± 1.34	–4.19–2.72		
Height SDS			111	
First visit	–0.46 ± 1.28	–4.47–2.36		
Last visit	–0.45 ± 1.31	–4.45–3.02		
BMI SDS			111	
First visit	0.24 ± 1.18	–2.09–3.07		
Last visit	0.17 ± 1.20	–2.09–3.11		
Growth velocity SDS	0.21 ± 1.32	–3.38–4.27	74	

BMI: body mass index; **SD:** standard deviation; **SDS:** standard deviation score; **n:** number of patients.
Note: Growth velocity was evaluated in 74 untreated children after excluding those with factors that could affect growth (e.g., epiphyseal closure, growth-suppressing medications, Down syndrome, prior chemotherapy).

Table 2. Comparison of demographic and clinical characteristics among outcome groups

Variable	Normalized n = 45 (%)	Stable n = 49 (%)	Progressed n = 17 (%)	p
Sex★				0.725
Female	31 (68.9%)	36 (73.5%)	12 (70.6%)	-
Male	14 (31.1%)	13 (26.5%)	5 (29.4%)	-
Age at diagnosis (years)	7.9 ± 3.9	7.8 ± 4.6	10.7 ± 4.5	**0.049**
Follow-up duration (years)	0.89 ± 0.42	0.79 ± 0.54	0.99 ± 0.76	0.365
Baseline TSH (mIU/L)	6.64 ± 1.09	7.15 ± 1.36	7.67 ± 1.27	**0.012**
Baseline fT4 (ng/dL)	0.91 ± 0.18	0.86 ± 0.13	0.80 ± 0.12	0.058
Family history of thyroid disease ★	24 (53.3%)	17 (34.7%)	11 (64.7%)	0.090
Hashimoto's thyroiditis †	5 (11.1%)	6 (12.2%)	8 (47.1%)	**0.005**
Idiopathic etiology †	32 (71.1%)	32 (65.3%)	6 (35.3%)	**0.030**
Use of medications affecting thyroid function (VPA etc.) †	2 (4.4%)	2 (4.1%)	1 (5.9%)	1.000
Obesity †	2 (4.4%)	4 (8.2%)	3 (17.6%)	0.236
BMI SDS	0.24 ± 1.07	0.08 ± 1.27	0.26 ± 1.33	0.766
Urinary iodine status (n = 39) †	Normalized n = 16 (%)	Stable n = 19 (%)	Progressed n = 4 (%)	0.823
Severe deficiency	0 (0%)	1 (5.3%)	0 (0%)	
Moderate deficiency	0 (0%)	1 (5.3%)	0 (0%)	
Mild deficiency	4 (25.0%)	2 (10.5%)	2 (50.0%)	
Optimal	8 (50.0%)	8 (42.1%)	2 (50.0%)	
Above requirement	2 (12.5%)	3 (15.8%)	0 (0%)	
Excessive	2 (12.5%)	4 (21.1%)	0 (0%)	

Continuous variables were analyzed using one-way ANOVA with Tukey HSD post-hoc test. Categorical variables were analyzed using Pearson's Chi-Square (★) or Fisher's Exact test (†), depending on expected cell counts. Statistical significance was set at $p < 0.05$. Bold values indicate significance.
SH: subclinical hypothyroidism; HT: Hashimoto's thyroiditis; TSH: thyroid-stimulating hormone; fT4: free thyroxine; BMI: body mass index; SDS: SD score; VPA: valproic acid.

Table 3. Comparison of HT and Non-HT SH Groups

Variable	HT group n = 19	Non-HT group n = 92	p value

Age at first visit (years)★	**11.5 ± 3.5**	7.6 ± 4.3	**< 0.001**
Age at last visit (years)★	**12.4 ± 3.7**	8.5 ± 4.3	**< 0.001**
Female, n (%)†	**15 (78.9%)**	48 (52.2%)	**0.013**
Baseline TSH (mIU/L)★	7.14 ± 1.27	7.00 ± 1.29	0.681
Follow-up duration (years)★	0.88 ± 0.60	0.85 ± 0.52	0.853
Became euthyroid†	5 (26.3%)	40 (43.5%)	**0.048**
Persistent SH†	6 (31.6%)	43 (46.7%)	0.484
Required levothyroxine†	8 (42.1%)	9 (9.8%)	**0.005**
Main reasons for treatment	n = 8 (%)	n = 9 (%)	
TSH > 10 mIU/L	2 (25.0%)	5 (55.6%)	-
Low fT4	2 (25.0%)	1 (11.1%)	-
Short stature	-	2 (22.2%)	-
Weight loss / poor appetite	-	1 (11.1%)	-
Goiter	3 (37.5%)	-	-
Goiter + TSH > 10	1 (12.5%)	-	-

Continuous variables were analyzed using the independent-samples t-test; categorical variables were analyzed using Pearson's chi-square test or Fisher's exact test when appropriate; $p < 0.05$ was considered statistically significant.
HT: Hashimoto's thyroiditis; SH: subclinical hypothyroidism; TSH: thyroid-stimulating hormone; fT4: free thyroxine; BMI: body mass index; SDS: SD score.

Table 4. Treatment requirement according to baseline TSH categories

Variable	**TSH ≤ 7.5 mIU/L n = 74 (%)**	**TSH > 7.5 mIU/L n = 37 (%)**	**Total n = 111 (%)**	**p / OR**
No treatment n (%)	67 (90.5%)	27 (73.0%)	94 (84.7%)	–
Treatment initiated n (%)	7 (9.5%)	10 (27.0%)	17 (15.3%)	0.015[1] / 0.024[2] OR = 3.55 (1.22–10.28)
Total n (%)	74 (66.7%)	37 (33.3%)	111 (100%)	–

[1] Pearson's chi-square test; [2] Fisher's exact test (used due to small expected cell counts). Likelihood ratio and linear-by-linear association tests also supported the results. Odds ratio (OR) with 95% confidence interval (CI) was reported. $p < 0.05$ was considered statistically significant.
TSH: thyroid-stimulating hormone; OR: odds ratio; CI: confidence interval.

Table 5. Evaluation of Baseline and Final TSH Means According to BMI Groups

Variable	**Underweight n = 2 (1.8%)**	**Normal n = 79 (71.2%)**	**Overweight n = 21 (18.9%)**	**Obese n = 9 (8.1%)**	**p[1]**
Baseline TSH (mIU/L)	6.02 ± 1.06	7.09 ± 1.31	6.85 ± 1.11	7.10 ± 1.45	0.614
Final TSH (mIU/L)	6.70 ± 1.03	5.48 ± 2.17	4.66 ± 2.04	7.70 ± 3.91	**0.012**
p[2] (Paired t-test)	0.727	< 0.001	< 0.001	0.648	-

[1] One-way ANOVA (post-hoc: Tukey HSD).
[2] Paired samples t-test.
Levene's test confirmed homogeneity of variances (p = 0.353).
Bold values indicate statistical significance (p < 0.05).
BMI: body mass index;**TSH:** thyroid-stimulating hormone;**SDS:** standard deviation score; **CI:** confidence interval.

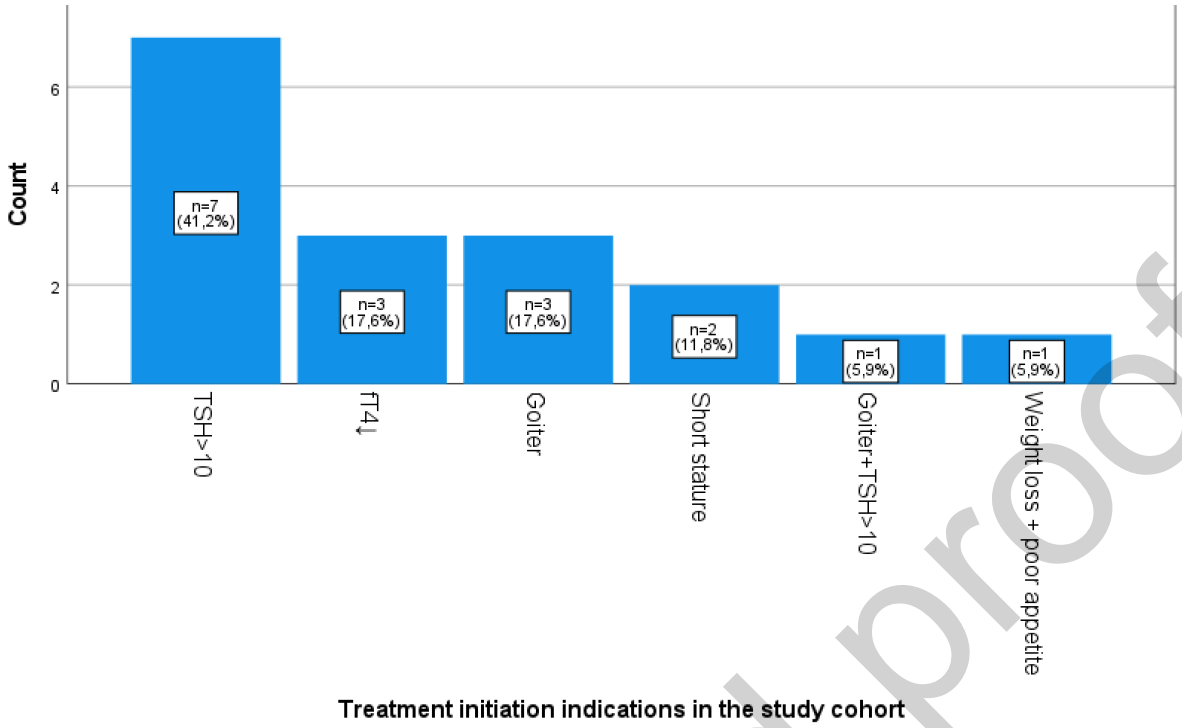

Figure 1. Reasons for initiation of treatment in the study cohort