Prevalence and Determinants of True Thyroid Dysfunction Among Pediatric Referrals for Abnormal Thyroid Function Tests

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Abstract

Background/Aims. Abnormalities in thyroid function tests (TFTs) are a common referral reason for pediatric endocrine evaluation. However, a sizable proportion of these laboratory abnormalities do not warrant therapy or endocrine follow-up. The objectives of this study were (*a*) to evaluate the prevalence of true thyroid dysfunction among pediatric endocrinology referrals for abnormal TFTs; (*b*) to identify the historical, clinical, and laboratory characteristics that predict decision to treat. *Methods*. This was a retrospective chart review of patients evaluated in pediatric endocrinology office during a weekly clinic designated for new referrals for abnormal TFTs in 2010. *Results*. A total of 230 patients were included in the study. Median age at referral was 12 years (range = 2-18); 56% were females. Routine screening was cited as the reason for performing TFTs by 33% patients. Majority was evaluated for hypothyroidism (n = 206). Elevated thyroid-stimulating hormone was the most common referral reason (n = 140). A total of 41 out of 206 patients were treated for hypothyroidism. *Conclusions*. Prevalence of hypothyroidism was 20%. Thyroid follow-up was not recommended for nearly one third of the patients. Among all the factors analyzed, an elevated thyroid-stimulating hormone level and antithyroglobulin antibodies strongly correlated with the decision to treat (*P* < .005).

Introduction

Thyroid function tests (TFTs) are among the most commonly performed endocrine laboratory investigation in the pediatric age group. An interesting phenomenon has been the increase in the use of TFTs as a diagnostic tool over the past several years. Although no US study has specifically investigated this phenomenon, a recent publication from Australia showed a 51% increase in orders for TFTs by general practitioners between 2001-2002 and 2010-2011 despite no change in the incidence of thyroid disease in the same population. This translated in approximately 2.4 million more TFT orders when compared to the prior decade.[1] Multiply this number by the cost of performing TFTs and the financial impact of this change is rather staggering.[2,3] Symptoms of hypothyroidism are rather nonspecific, and this may be one of the reasons for frequent ordering of TFTs. Additionally,

some of these tests are ordered in situations such as evaluations for constipation or fatigue when the probability of thyroid dysfunction causing the symptoms is rather low.[3,4] Findings of "abnormal" TFT results or thyroid examination frequently prompt referral to a pediatric endocrinologist for evaluation and possible treatment. There are however scant data on the outcomes of these referrals, especially when the abnormalities in TFTs are rather mild. While some of these patients do have a

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thyroid disorder requiring treatment, the majority represents physiological variation in TFTs or laboratory interferences and not true thyroid dysfunction.[5,6]

The aims of our study were (*a*) to evaluate the prevalence of true thyroid dysfunction among children referred for abnormal TFTs and (*b*) to ascertain the historical, clinical, and laboratory characteristics that predict decision to treat.

Methods

Our pediatric endocrinology division is located in a 202-bed tertiary care children's hospital and caters to a mix of suburban and inner-city population. Due to the increased number of referrals by the hospital or community pediatricians and other subspecialists for abnormal TFTs, a once weekly half-day clinic session (named new patient clinic [NPC]) was started in 1992. The clinic is staffed by an endocrine fellow (with or without an endocrine nurse practitioner) under the supervision of 1 of 7 pediatric endocrinologists.

Patients evaluated between January 1, 2010, and December 31, 2010, at the NPC were identified retrospectively by an outpatient appointment scheduling database search using the ICD-9 codes mentioned below. Electronic charts for these patients were then reviewed to identify patients who met inclusion and exclusion criteria.

Inclusion criteria:

1. Age at evaluation: 2 to 18 years
2. Have a diagnosis of nonspecific abnormal results of function study of thyroid (ICD-9 code 794.5) and/or Goiter, unspecified (ICD-9 code 240.9) and/or Unspecified disorder of the thyroid (ICD-9 code 246.9), thyroid nodule (ICD-9 code 241.0)

Exclusion criteria:

1. Known thyroid disorder at initial presentation
2. Patient on thyroid hormone replacement or antithyroid medication at initial evaluation

Collected data included demographic data (age at initial endocrine evaluation and sex), clinical history (indication for thyroid testing, reason for endocrine referral, presence or absence of symptoms suggestive of thyroid disease, personal or family history of autoimmunity, past medical history, and current medications), pertinent physical exam findings (body mass index [BMI], presence or absence of goiter, and Tanner stage), initial and follow-up laboratory studies and recommendations. BMI-*z* score and BMI percentile based on CDC 2000 growth charts were recorded. The study was approved by the institutional review board.

TFTs ordered by the referring physicians were performed at a variety of commercial laboratories utilizing different assays. The majority of these laboratories used adult reference ranges when reporting results. Repeat TFTs were performed in several patients before starting treatment, and most of these follow-up tests were performed at our institution's core laboratory. During the period of the study, assays used and the reference ranges for the commonly requested TFTs at our laboratory are as follows:

1. TSH (thyroid-stimulating hormone): Roche Diagnostics electrochemiluminescence immunoassay (ECLIA) using sandwich principle. Limits of detection: 0.005 to 100 μIU/mL and the normal range being 0.27 to 4.2 μIU/mL.
2. Total T4 (tetra-iodo-thyronine): Roche Diagnostics ECLIA using competition principle. Limits of detection: 0.42 to 24.9 μg/dL and the normal range being 4.5 to 11.7 μg/dL.
3. Free T4: Roche Diagnostics ECLIA using competition principle. Limits of detection: 0.023 to 7.77 ng/dL with the normal range being 0.93 to 1.7 ng/dL.
4. Total T3 (Tri-iodo-thyronine): Roche Diagnostics ECLIA using competition principle. Limits of detection: 0.195 to 6.51 ng/mL with the normal range being 0.8 to 2 ng/mL.
5. Anti-TPO (antithyroid peroxidase) and anti-Tg (anti-thyroglobulin) antibodies: Siemens Healthcare Diagnostics Products' solid-phase, enzyme labeled, chemiluminescent sequential immunometric assay with reference range for anti-TPO antibody being 0 to 34 IU/mL and for anti-Tg antibody being 0 to 40 IU/mL.

The decision to start therapy or the decision to treat was based on the clinical judgment of the attending physicians in the NPC. There was no specific protocol in place to guide whether a patient should receive therapy.

Statistics

Laboratory test results were analyzed as continuous variables (eg, TSH), categorical variables (eg, antithyroid antibody titers, often measured at outside laboratories with different reference ranges), or ordinal variables (eg, total and free T4 levels and T3 levels interpreted as low, normal, or high based on laboratory reference range) as applicable. The χ^2 test was used to assess categorical variables. Continuous clinical variables were expressed as the median/mean and range, and comparisons were made
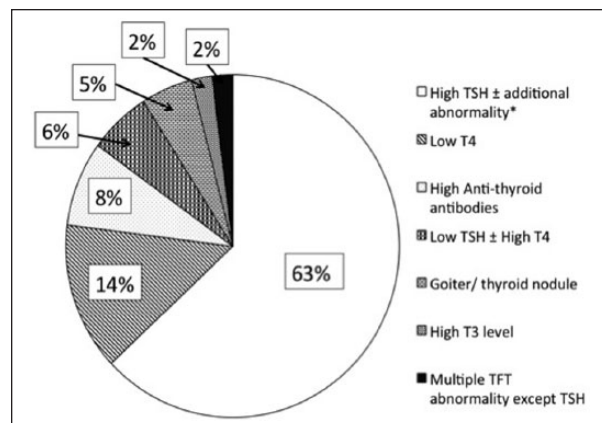
Figure 1. Pie diagram showing the various TFT abnormalities for which endocrine referral was made.

with the Mann-Whitney *U* test or Wilcoxon signed-rank test. A 2-tailed *P* value <.05 was considered to be statistically significant. Linear regression and stepwise multiple regression analysis was performed with thyroxine treatment as the dependent variable and several independent variables listed in Table 2. Analyses were performed using JMP IN 7.0.2 software (SAS Institute, Cary, NC).

Results

Demographic and Clinical Factors Associated With the Referral to the NPC

A total of 230 patients were included in the study. Referred patients presented with a wide spectrum of abnormalities in TFTs (Figure 1). Detailed patient characteristics including salient features of their medical history and physical examination are presented in tabulated form (Table 1). Most of the patients (n = 140, 64%) were referred for elevated TSH with/ without additional abnormalities. While about 45% patients reported symptoms associated with thyroid disease (Table 1), overall 67% patients underwent TFTs for diagnostic purposes (due to reported symptoms of fatigue, weight gain, etc, or signs of goiter or due to other historical features including psychiatric diagnoses or treatment with psychotropic medications; Figure 2). In a significant number of referrals (n = 75, 33%), TFTs were performed as a part of routine annual examination (Figure 2). A large proportion of patients (n = 100, 43%) had no significant past medical history. Nearly half of the patients (n = 99, 43%) were prepubertal and a similar proportion had a family history of autoimmune thyroid or other diseases (n = 111, 48%).

Referral for Evaluation of Hypothyroidism

Majority of the patients (n = 212) were evaluated for hypothyroidism. Six of these patients were considered

Table 1. Initial Patient Characteristics (N = 230) Including Salient Features of History and Physical Examination.

Characteristic	Data
Age (years) at initial evaluation, median (range)	12 (2.1-17.9)
Females	56%
Symptoms suggestive of thyroid disease	45%
Personal history of autoimmunity	No: 98%
	Yes: 2%
Family history of autoimmunity	None: 51%
	Yes, thyroid disease only: 41%
	Yes, thyroid and other autoimmune diseases: 5%
	Yes, other autoimmune diseases: 3%
Medication history	Not on medications: 58%
	On medications with no known effect on TFTs: 30%
	On lithium therapy: 4%
	On other medications affecting TFTs[a]: 8%
Body mass index (BMI)[b]	<85th percentile: 57%
	85th-95th percentile: 13%
	95th-99th percentile: 21%
	>99th percentile: 9%
Tanner stage	1: 43%
	2: 8%
	3: 4%
	4: 7%
	5: 20%
	Data not available: 18%
Goiter	Absent: 81%
	Present: 19%

Abbreviation: TFT, thyroid function test.
[a]These medications included escitalopram, quetiapine, sertraline, carbamazepine, valproic acid, divalproex sodium, and ranitidine.
[b]BMI data not available for 6 subjects.

high risk for hypothyroidism. Of these 4 patients had Down syndrome, 1 patient had received neck radiation for Ewing sarcoma of cervical spine, and 1 patient had received 4 cycles of chemotherapy for Hodgkin's disease of cervical spine. All these 6 patients were referred for an elevated TSH value and received thyroid hormone replacement for a diagnosis of acquired primary hypothyroidism. These patients are excluded from subsequent analysis.

For the purpose of this article, the remaining 206 patients are divided into subgroups based on their TSH levels.

Elevated TSH Level (n = 140/206). Median TSH level at the time of referral was 6.24 μIU/mL (4.3-57.94). Repeat TFTs were performed in 105 of 140 patients at their first visit or

Table 2. Comparison of Clinical and Laboratory Characteristics of Patients Treated for Hypothyroidism and Those Not Treated.

	Patients Evaluated for Hypothyroidism (N = 206)		
	Patients Treated (n = 41)	Patients Not Treated (n = 165)	P
Age at evaluation (in years)[a]	12.1 (2.1-17.4)	12.2 (2.3-17.9)	NS
Females	76%	53%	.0066
Symptoms suggestive of hypothyroidism	44%	47%	NS
Family history of autoimmunity	63%	45%	.0423
BMI-z score[a]	0.91 (−3.51 to 2.61)	0.78 (−2.84 to 3.82)	NS
BMI percentile[a]	83.6% (0 to 99.5)	78.2% (6.9 to 100)	NS
Tanner stage	Tanner 1: 44%	Tanner 1: 42%	NS
	Tanner 2: 12%	Tanner 2: 9%	
	Tanner 3: 2%	Tanner 3: 3%	
	Tanner 4: 7%	Tanner 4: 8%	
	Tanner 5: 17%	Tanner 5: 21%	
	Data not available: 17%	Data not available: 17%	
Goiter	39%	15%	.0009
Decision making TSH value (µIU/mL)[a]	10.45 (4.3-57.94)[b]	3.5 (0.65-9)	<.0001
T4 and/or free T4 value	Normal: 70%	Normal: 77%	NS
	Low with a normal TSH: 0%	Low with a normal TSH: 18%	
	Low with TSH over 4.2 µIU/mL: 30%	Low with TSH over 4.2 µIU/mL: 5%	
Anti-thyroglobulin antibody	Positive: 68%	Positive: 19%	<.0001
	Negative: 17%	Negative: 56%	
	Data not available: 15%	Data not available: 25%	
Anti-thyroperoxidase antibody	Positive: 56%	Positive: 15%	<.0001
	Negative: 29%	Negative: 58%	
	Data not available: 15%	Data not available: 27%	

Abbreviations: NS, not significant; BMI, body mass index; TSH, thyroid-stimulating hormone.
[a]Data expressed as median (range); P value based on unpaired t test or χ^2 test.
[b]N = 40. One patient treated for goiter with a TSH value of 4.17 µIU/mL excluded while calculating median TSH value of treated patients.
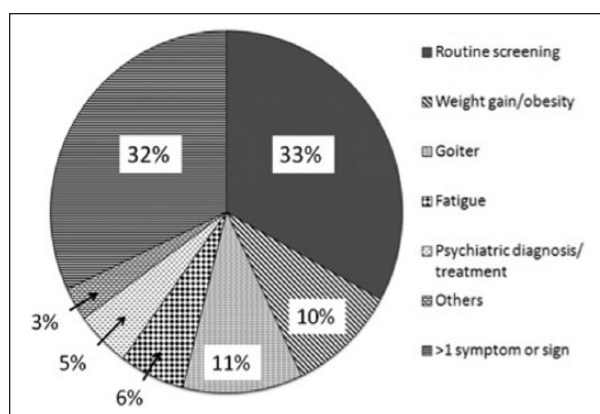

Figure 2. Pie chart summarizing the different reasons for performing thyroid function tests as stated in the referral or by patients at initial endocrine visit.

soon after. Median TSH value at referral for these 105 patients was 6.71 µIU/mL (4.31-24.32). Median follow-up TSH value was 4.13 µIU/mL (1.17-34.4), indicating a decrease of almost 2 µIU/mL (−9.16 to 15.63). While 85 of the 105 patients showed some decrease in TSH level, the follow-up TSH was within the laboratory reference range for 54 patients (51%). Repeat TFTs were generally done after an interval of 6 to 8 weeks from the initial labs. Anti-TPO and/or anti-Tg antibody results were available for 119 patients, and a positive titer for at least one antibody was present in 46 patients (39%).

Normal TSH Level (n = 66/206). These patients had a normal TSH level (median = 1.82 µIU/mL [0.38-4.74]); however, they had other abnormalities in TFTs: low free T4 (n = 20), low total T4 (n = 8), low total T3 (n = 3), positive antibodies (n = 18), goiter/thyroid nodules (n = 12), or a combination of these findings (eg, goiter and positive antibodies, n = 4). Five patients were diagnosed with thyroid binding globulin deficiency; none had hypothyroidism. Both total and free T4 were low in one patient, which normalized on repeat testing.

Characteristics of the Patients That Received Thyroxine Treatment

Only 20% (41/206) of all referrals for hypothyroidism were diagnosed with primary hypothyroidism and treated with levothyroxine replacement. Thirty-eight patients (92%) were referred for an elevated TSH with/without other abnormalities, and 12 of these also had a low T4. Three patients with normal initial TSH levels were referred for positive antithyroid antibodies. Interestingly, 2 out of the 3 patients had an elevated TSH on repeat testing. The third patient was a 17-year-old asymptomatic girl, who had a family history of autoimmune thyroid disease, was Tanner stage 5 on pubertal exam, and had a palpable goiter, a high normal TSH value (4.17 μIU/mL), and a normal T4 level. She was treated primarily to decrease the size of her goiter. Table 2 summarizes the characteristics of treated and untreated patients.

A large proportion of the treated patients were prepubertal (44%), though this was not different compared to the untreated group (42% prepubertal) and similar to the overall referred patients. Stepwise regression analysis with thyroxine treatment as the dependent variable and female sex, family history of autoimmunity, presence of goiter, a higher TSH level (median 10.45 μIU/mL in the treated group vs 3.5 μIU/mL in the untreated group), and the presence of anti-Tg and anti-TPO antibodies showed association with treatment. However, elevated TSH level and positive anti-Tg antibody titers were the only 2 independent predictors associated with thyroxine treatment ($P < .005$). Interesting, no correlation was found between positive anti-TPO antibodies and treatment, and further analysis confirmed that the lack of association was independent of data availability.

Follow-up and Outcome

Endocrine follow-up was recommended for all 41 patients diagnosed with hypothyroidism. Among the 165 patients not started on treatment, endocrine follow-up was recommended for 42 patients (25%), and periodic (annual or semi-annual) follow-up TFTs with the primary care physician were recommended for 45 patients (27%). Additionally, 4 patients with single or multinodular thyroid disease were referred to pediatric otorhinolaryngologist/thyroidologist for a surgical consultation. While follow-up data were not available for 2 patients, one patient was recommended total thyroidectomy for extensive nodular disease. No intervention was advised for a patient with multiple colloid cysts.

Among the patients who were not treated, the subgroup to whom thyroid screening follow-up was recommended (n = 91) had similar median age, gender distribution, and BMI-*z* scores to those with no recommended follow-up (n = 74; see Table 3). Patients in both groups also reported symptoms suggestive of thyroid disease at a similar frequency. Of note, however, patients in whom follow-up was recommended were more likely to have a positive family history of autoimmunity, goiter on physical examination, positive anti-TPO and anti-Tg antibodies, and a higher median TSH value (3.8 vs 2.91 μIU/mL) ($P < .05$ for all parameters).

Some theoretical risk factors for thyroid disease were present in a small proportion of patients not recommended follow-up. While 3 patients had goiter, they did not have thyroid antibodies or family history of autoimmunity. Of those who did not have goiter, 4 patients had a family history of thyroid disease and evidence of thyroid autoimmunity (3 with anti-Tg alone and 1 with anti-Tg and anti-TPO). Both antithyroid antibodies were positive in 2 additional patients but had no family history of autoimmunity. While antibody titers were less than 3 times the upper limit of normal in 3 patients, in the other 3 patients, titers were markedly elevated. Additionally, 18 patients only had a family history of autoimmunity.

Referral for Evaluation of Hyperthyroidism

Eighteen patients (8% of all study patients) were referred for a low TSH and/or high T4 or high T3 value and a concern for hyperthyroidism. Of these, 6 patients (33%) had a suppressed TSH (TSH value <0.1 μIU/mL) and were evaluated for hyperthyroidism. Four (22%) patients were diagnosed with Graves' disease (based on a combination of clinical symptoms, TFTs, and presence of thyroid-stimulating immunoglobulins and/or TSH receptor antibodies). Two patients received treatment (both were treated medically with antithyroid medications), and 2 were closely monitored without treatment due to lack or minimal symptoms. TSH value in these patients normalized 4 months and 1 year after the initial visit, respectively.

Patients referred for a low but nonsuppressed TSH (TSH >0.1 μIU/mL) and/or isolated elevated T4 value (n = 8) were grouped together. Repeat TFTs were performed for 6 of these patients and were normal, including negative antithyroid antibodies. None of these patients required treatment. Follow-up annual TFTs were recommended for 5 patients who had a family history of autoimmunity. A third subgroup of patients (n = 4) had an elevated T3 level (compared to laboratory reference range) as the only laboratory abnormality. They had a normal TSH and total/free T4 level. When compared to age-appropriate reference ranges,

Table 3. Comparison of Clinical and Laboratory Characteristics of the Patients Referred for Hypothyroidism Evaluation But Not Treated (n = 165/206) Based on Their Follow-up Recommendations.

Characteristic	Thyroid Follow-up Not Recommended (n = 74)	Thyroid Follow-up Recommended (n = 91)	P
Age (years)[a]	11.88 (2.33-17.83)	12.5 (2.33-17.9)	NS
Females	46%	58%	NS
BMI-z score[a]	1.22 (−1.37 to 3.82)	0.69 (−2.84 to 3.38)	NS
Symptoms suggestive of hypothyroidism present	54%	41%	NS
Family history of autoimmunity present	31% (n = 22/71)[b]	56% (n = 48/86)[b]	.0018
Goiter present	4%	23%	.0006
Decision making TSH level (µIU/mL)[a]	2.91 (0.65-6.01) (n = 74)[b]	3.8 (0.78-9.04) (n = 90)[b]	.0125
Anti-Tg antibody positive	13% (n = 6/47)[b]	32% (n = 25/77)[b]	.0140
Anti-TPO antibody positive	6% (n = 3/48)[b]	29% (n = 21/73)[b]	.0024

Abbreviations: NS, not significant; BMI, body mass index.
[a]Data expressed as median (range); *P* value based on Wilcoxon test or χ^2 test.
[b]N mentioned when data were not available for all subjects.

their T3 values were normal. None of these patients required treatment and no follow-up thyroid testing was recommended.

Discussion

Our study found that the majority of patients referred for abnormal TFTs did not have thyroid disease requiring treatment. Only 20% of the patients referred to rule out hypothyroidism were found to have true thyroid dysfunction and treated. Among the historical, clinical, and laboratory characteristics evaluated, the decision to treat was independently associated with elevated TSH level and elevated anti-Tg antibody only. No thyroid follow-up was recommended for 36% of patients, indicating they had minimal-mild abnormalities in TFTs of no clinical significance. Explanation of the findings and reassurance by the primary pediatrician could have sufficed in these cases and a formal endocrine consultation was likely not necessary.

Majority of those referred for concern of hypothyroidism were referred for an elevated TSH. Most of the commercial laboratories and frequently core laboratories of hospitals do not provide TSH reference ranges for children. Although TSH reference ranges for children may vary somewhat between individual laboratories, TSH values for prepubertal children have been shown to be somewhat higher than adults.[7] Hence, several of these minimal TSH "elevations" may in fact be normal for the patient. Follow-up TSH was normal in over 50% of patients who underwent repeat TFTs (often at a different laboratory) after about 6 to 8 weeks of the initial testing. There are several possible explanations for this variation in TSH value including difference in laboratory assays, presence of interfering antibodies (such as human anti-mouse antibody or HAMA), circadian variability of

TSH (early morning TSH value being statistically higher than afternoon TSH value), and effect of any intercurrent illness.[8,9] Those who persisted to have an elevated TSH were considered for treatment, and 38 of all 41 patients treated for hypothyroidism were from this group.

Of the 66 patients who were referred for a non-TSH-related reason, the vast majority did not receive treatment. Most of the patients with low free T4 values had normal results when repeated by a different analog assay or with equilibrium dialysis. Since most of the commercial laboratory assays for free T4 are direct analog immunoassays that may be affected by binding protein concentrations, falsely low results may be obtained.[10] While total T4 is an otherwise robust assay, it can be affected by congenital or acquired variations in binding proteins as in thyroxine binding globulin deficiency—a benign condition that does not require treatment.

In our cohort, median age, BMI-*z* score, and Tanner stage distribution of the patients diagnosed and treated for hypothyroidism was not statistically different than the ones not treated (Table 2). Interestingly, although acquired thyroid disease (mostly autoimmune or Hashimoto's thyroiditis) is considered a disease of the adolescent age group, nearly half of the treated patients were prepubertal. This could either reflect a shift in the disease epidemiology or increased testing in this age group. Symptoms associated with thyroid disease were reported equally by both treated and untreated groups, reflecting their nonspecificity, especially in subclinical hypothyroidism as in the majority of our patients (29 of 41 patients).

Elevated TSH level as an independent factor associated with thyroxine treatment was not surprising as TSH is the most sensitive and usually the earliest marker of thyroid dysfunction. However, among the other factors, thyroxine treatment was also independently associated

with positive anti-Tg antibodies rather than anti-TPO antibodies. This was an interesting finding as large population-based studies have found anti-TPO antibodies as a more specific marker for Hashimoto thyroiditis.[11] Etiology of the difference between our findings and this classic teaching is unclear; however, in a study on natural history of euthyroid Hashimoto thyroiditis, anti-Tg antibodies (and goiter) appeared before the appearance of anti-TPO antibodies and elevation in TSH.[12] The relative young age and prepubertal stage of a large number of patients in our cohort makes this a possible explanation. If this finding is reproduced in other studies, it may provide valuable information on pathogenesis of Hashimoto thyroiditis.

For patients not started on thyroxine treatment, follow-up thyroid studies were more often recommended for patients with goiter, positive family history of autoimmunity, positive anti-TPO and anti-Tg antibodies, and high TSH level. This indicates that these patients were considered to be at risk for developing hypothyroidism. Interestingly, patients for whom thyroid follow-up was not recommended reported more symptoms compared to those for whom thyroid follow-up was recommended, though the difference was not significant. This likely points toward the nonspecific nature of symptoms associated with hypothyroidism. A small number of patients for whom further thyroid follow-up was not recommended had similar features with the patients for whom follow-up was recommended, indicating some practice variation between the treating physicians.

No follow-up was recommended for approximately one third of the patients. Guidelines from national pediatric or endocrine associations and societies on performing TFTs in otherwise healthy children are lacking. The US Preventive Task Force in its statement (published January 2004) on screening for thyroid disease concluded that there is insufficient evidence to recommend for or against routine screening for thyroid disease in adults.[13] Some studies have reported detecting subclinical thyroid disease during routine annual health screening of asymptomatic adult patients.[14] However, the cost-effectiveness of such a screening approach is yet to be established before its population-wide use. Second, natural course and treatment of subclinical hypothyroidism in children is still a controversial issue even among endocrinologists, and a detailed discussion on this topic is beyond the scope of this research study. Until further studies support the use of routine TFTs, providers should probably exercise restraint in ordering TFTs when taking care of otherwise healthy and asymptomatic patients at low risk of thyroid disease. Certainly the finding of a mildly elevated TSH warrants a repeat

determination prior to referral, as in our study, almost half of patients had a normal TSH on the repeat analysis.

The number of patients referred for evaluation of hyperthyroidism in our cohort was much smaller compared to those evaluated for hypothyroidism. This likely represents the fact that hypothyroidism is more common than hyperthyroidism. It is also possible that since hyperthyroidism, if strongly suspected based on clinical symptoms and laboratory findings, was evaluated on a more urgent basis rather than evaluation as a next available appointment and hence probably underrepresented in our cohort (similar to patients with overt hypothyroidism). Of the patients with laboratory results indicative of hyperthyroidism (suppressed TSH level with elevated T4 and/or T3), Graves' disease was the most common etiology (4 of 6 patients with hyperthyroidism) and treatment decision was based on both clinical and biochemical findings. Hashitoxicosis and subacute thyroiditis was diagnosed in only one patient each. Due to the small number of these patients, significant inferences could not be drawn for the hyperthyroid group.

One of the limitations of our study is that our cohort may not have included patients with marked abnormalities in TFTs who likely were often seen at a more urgent appointment rather than on the next available appointment (during our once a week clinic). Hence, our findings may be more applicable for patients with mild TFT abnormalities. Our findings suggest that patients with mild abnormalities in TSH and/or T4, no family history of autoimmunity, no goiter on physical examination, and negative antithyroid antibodies do not need routine thyroid follow-up and may not need thyroid screening in the first place. This finding reflects the need for further studies on the natural history of mild TFT abnormalities, so that evidence-based management guidelines for endocrinologists and pediatricians can be formulated. Our results provide an initial assessment of this trend of increasing endocrine referrals for abnormal TFTs and highlight the areas that need further studies. There is a need to formulate better guidelines to reduce unnecessary thyroid testing and referrals.

Author Contributions

AL: Contributed to conception and design; contributed to analysis; drafted the manuscript; critically revised the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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