Profile of necessary thyroid tests in a Colombian university hospital

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Abstract

Introduction: There are no clear clinical guidelines for requesting thyroid tests in hospitalized patients. The necessity and profile of requested tests in hospitalized patients at the San Vicente Foundation University Hospital were evaluated.

Methods: This retrospective study included patients over 14 years of age who were nonpregnant and hospitalized at the Hospital Universitario de San Vicente Fundación. A total of 351 records were evaluated in the clinical history system, six necessity groups were defined: categories 1 to 4 were considered necessary test requests, and 5 and 6 were considered unnecessary test requests.. Demographic and clinical variables were recorded. Quantitative statistical variables were evaluated with the Mann-Whitney U test, and qualitative variables were evaluated with Pearson's chi square and Fisher's tests.

Results: Normal values were obtained for 67% of the measured thyroid stimulating hormone (TSH), 80% of the measured thyroxine (T4) and 53% of the measured triiodothyronine (T3). The most frequent abnormality in TSH was an elevation, observed in 24% of tests, the most frequent abnormality for free T4 (T4L) was a decline, observed in 11.5% of tests, and the most frequent abnormality for T3 was an elevation, as observed in 27% of tests. TSH ≤ 0.1 was found in 3.5% and ≥ 20 in 3.9% of tests. Of the 60 patients with elevated TSH, 75% had values between 5 and 9.99 mUI/mL; 11.5% had T4L values ≤ 0.7 ng/dL, and 8.6% had T4L values ≥ 1.48. In total, 95% of T4L measured in the unnecessary category was normal.

Conclusions: Requests for necessary thyroid tests during hospitalization should be improved. An initial approach is proposed only with TSH. **(Acta Med Colomb 2019; 44. DOI: https://doi.org/ 10.36104/amc.2019.1057).**

Key words: *thyroid tests, relevance, laboratory studies, hypothyroidism, thyroid stimulating hormone*.

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Introduction

Thyroid disease (TD) comprises a broad spectrum of entities that oscillate between subclinical forms and extreme manifestations of myxedema coma and thyroid storm (9-12). Correct detection impacts the choice and initiation of appropriate treatment, but diagnosis is not always easy given variable clinical presentation on admission, such as heart failure, heart arrhythmia, hyponatremia, myopathy, and sensory alterations, among others. The increasing volume of TD incidence, its complications, and hospitalizations generated lead to high health budget costs (1, 2).

To our knowledge, in Colombia, there is little data that address the epidemiology of TD and especially diagnostic approaches to TD during general hospitalization.

TD is diagnosed by thyroid function tests (TFTs). Reports from the international literature indicate that testing necessity can fluctuate between 42 and 72%, generating high costs for the health system (1). The aim of this study was to characterize the profile of TFT requests and their necessity in a population of hospitalized, nonpregnant patients at the San Vicente Foundation University Hospital in Medellin, Colombia.

Methods

A descriptive, retrospective, cross-sectional study was conducted in patients over 14 years of age who were nonpregnant, hospitalized at the San Vicente Foundation University Hospital - Medellín and underwent TFTs between

January and May 2015.

Of the 351 records reviewed in the clinical history system, 231 patients met the inclusion criteria.

The requested TFTs were characterized according to number and requestor medical specialty. Then, the patients were grouped into six necessity groups defined by the researchers and in accordance with international standards (5,13), as follows: categories 1 to 4 were considered indicators of necessary requests, and categories 5 and 6 were considered requests for unnecessary tests (Table 1).

Demographic variables, pathological antecedents, previous TD, admission and discharge diagnoses, requestor specialty, medications used, thyroid test type and complementary test type were recorded.

The definition of normal for the thyroid tests was defined by institutional reference values: TSH, 0.35 to 4.94 mIU/mL; T4L 0.7 to 1.48 ng/dL; and total T3 0.58 to 1.59 ng/mL. TFTs were performed by chemiluminescence on the Abbott® ARCHITECT platform.

Information was obtained after prior authorization from the research committee of the San Vicente Foundation University Hospital and was collected from clinical laboratory records of the hospital and the respective medical records. The database was developed in Excel, and the statistical information was processed using SPSS version 19. Quantitative statistical variables were evaluated with the Mann-Whitney U test, qualitative variables were evaluated with Pearson's chi square and Fisher's tests. Statistical significance was considered $p<0.05$.

Results

Test requests were analyzed for 231 patients (125 (54.1%) women and 106 (45.9%) men) with a median age of 59 years (IQR 41-73) for women and 64 (IQR 43-73) for men.

Of the patients evaluated, 78.7% had no history of TD, and 80% had a history of nonthyroidal pathologies. In order of frequency, the nonthyroidal pathologies were hypertension (41%), diabetes mellitus (DM) (20%) and dyslipidemia (10%); the frequencies of coronary heart disease, congestive heart failure, depression, epilepsy, and chronic kidney disease were below 6%.

In the study patients, the use of drugs that potentially alter the binding of thyroid hormones to proteins was documented: 49% were administered enoxaparin, 18% were administered furosemide, and 18% were administered enoxaparin and furosemide combined.

TSH tests were ordered for 229 patients (99%), the most requested test. Isolated TSH tests were ordered for 55.4% of patients, followed by combined TSH and T4L tests for 37.9% of patients and combined TSH, T4L and T3 tests for 6.5% of patients (Figure 1).

In two patients (1%), the only initial test requested was T4L: one with a diagnosis of primary hypothyroidism and the other in whom medical history was not justified.

T3T was not ordered alone or in exclusive combination with TSH; however, TSH + T4 L + T3T tests were ordered for 15 patients. Of the patients with low TSH levels and simultaneous T3T measurements, four patients had high T3T levels, and one patient had normal T3T levels. Of the patients with high or normal TSH levels and simultaneous T3T measurement of (n: 10), nine patients had normal T3T levels, one patient had low T3T levels.

In 10 patients (4.3%), microsomal (anti-TPO) thyroid antibodies were measured as a complementary test, of which nine (90%) had altered TSH levels: high for six patients (5.03 - 303.8 mIU/ml) and low for three patients (0.0 - 0.3 mUI/mL). The positivity rate for requested anti-TPO tests was 60% (6/10), three with high TSH levels (50%) and three with low TSH levels (50%). Of the four patients who were anti-TPO negative, three had abnormal TSH levels, and one had a normal TSH level.

Values within normal limits were obtained for 67% of the TSH measured, 80% of the T4 measured and 53% of the T3 measured. For TSH, the most frequent abnormality was an elevation, observed in 24% of tests; for free T4, the most frequent abnormality was a reduction, observed in 11.5% of tests, and for T3, the most frequent abnormality was an elevation, observed in 27% of the tests (Figure 2).

Table 1. *Distribution of thyroid test request categories, according to necessity group (21).*

Category	Reason for request	Description
Group 1	Monitoring of previously known thyroid disease	Hypothyroidism, hyperthyroidism, thyroidectomy, and history of radioactive iodine therapy
Group 2	De novo thyroid disease clinic	Fatigue, intolerance to the cold, dry skin, weight gain, menstrual irregularities, goiter, bradycardia, delayed relaxation phase of deep tendon reflex, hair loss, fragile nails. tachycardia, irritability, involuntary weight loss, exophthalmos, fine tremor in hands, proximal muscle weakness and lack of concentration
Group 3	Image or clinical history (temporary hemianopia or other) suggesting pituitary tumor that compromises the thyroid axis at the central level.	
Group 4	Another reason justified by the international literature	Congestive heart failure (CHF), atrial fibrillation (AF), arrhythmia, cardiomyopathy, delirium, repeated miscarriages, autoimmune disease (DM1- DM LADA), pernicious anemia, psychiatric illness, macrocytic anemia, hypercholesterolemia, hyponatremia and elevated creatine kinase, and myopathies
Group 5	Another reason not justified by the international literature	
Group 6	No justified reason in the clinical history	

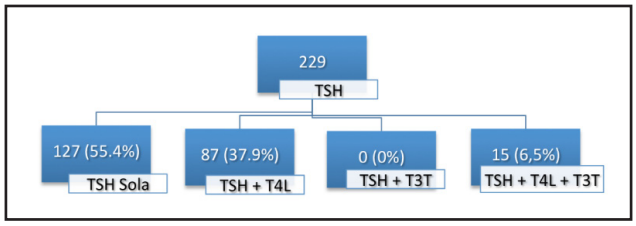

Figure 1. *Initial profile of requested TSH tests.*

Of the requested tests, 112 were considered necessary (48.5%), and 119 were considered unnecessary (51.5%) (Table 2). TSH was requested for 99% of the patients in this study and was normal in 67.9% and 68.1% of tests In the necessary and unnecessary categories, respectively. Tables 5 and 6 show the distribution of TSH and free T4 by subgroup (normal or abnormal) and according to necessity categories.

Within the necessity subgroups, 26.8, 17.3, 3.9 and 0.4% corresponded to categories 4, 1, 2 and 3, respectively. Within the unnecessary subgroups, 31 (26.1%) tests corresponded to category 5, and 88 (73.9%) corresponded to category 6 due to a lack of annotation of the reason for request in the clinical history.

In total, 23 different specialties requested TFTs, with general medicine (36.4%), internal medicine (35.9%) and psychiatry (5.6%) ordering the most tests. Other specialties, such as toxicology, cardiology, and neurology, among others, accounted for less than 4% of the requests.

The percentages of necessary tests requested by clinicians in general medicine, internal medicine and psychiatry were 45.2, 57.8 and 80.6%, respectively. Tests requested by clinicians in specialties such as endocrinology, orthopedics and otorhinolaryngology showed 100% necessity; however, these compose 0.4% of the total requests per specialty.

Clinicians in specialties such as neurology, infectious disease and critical care and intensive care (ICU) medicine ordered thyroid tests for 3.4, 1.7 and 2.1% of the patients, respectively, for a total of 15 requested thyroid profiles, with a percentage of necessity lower than 12.5%. Twelve (80%) of these requests were classified as unnecessary due to a lack of support in the clinical history (category 6), and three of them were classified as category 5 for reasons beyond the scope of this study.

Of the three specialties with the most TFT requests, a subgroup analysis was performed. While internists and psychiatrists most often chose TSH as their initial test (61%), general medicine clinicians chose TSH and T4L combined (48.8%) (Table 3).

In 31 patients (13%), thyroid tests were requested for justified reasons different from those supported by the literature (category 5), such as acute myocardial infarction (AMI) (10%) and cerebrovascular disease (CVD) (10%). Other justifications, such as sepsis, convulsive episodes, intoxication, lipophilia, and initiation of antituberculosis therapy, were found in less than 3% of cases.

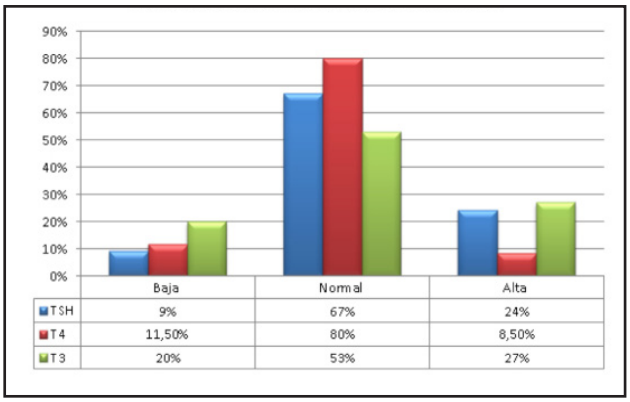

Figure 2. *Thyroid hormone test results. TSH reference ranges in mIU/mL (low < 0.35, normal 0.35 - 4.95, high > 4.94), T4L in ng/dL (low < 0.7, normal 0.7-1.48, high > 1.48), T3 in ng/mL (low <0.58, normal 0.58 - 1.59, high > 1.59).*

Of the 49 patients with a history of TD (21.2%), the TFT request necessity categories were distributed as follows: 37 (75.5%) in category 1, three (6.2%) in category 2, one (2%) in category 4 and 8 (16.3%) in category 6.

Discussion

To our knowledge, this is the first study of the necessity and characterization of TFT requests in Colombia. Previous studies in other countries have found that this necessity fluctuates between 42.5 and 72.4%, which agrees with our work. Necessity values can be improved after sensitization of medical personnel to criteria and clear indications for TFT requests, especially TSH levels as an initial thyroid test (1).

According to the literature, the LRs of TSH levels in hospitalized patients that best predict hyperthyroidism and hypothyroidism are TSH ≤ 0.1 (LR 7.7) and TSH ≥ 20 (LR 11.1), respectively (3). In the population evaluated, including patients with TSH levels greater than 10, only 10% of the TSH requests met these criteria (Table 4). Only one in five measurements of free T4 was abnormal, which confirms the importance of waiting for the TSH value to determine the need for subsequent T4 requests, especially in cases of hyperthyroidism or when there is a slight increase in TSH (less than 10).

In our study, TSH was the initial thyroid test requested in the majority of cases (99%), which is consistent with the international literature (1, 2,4-6) and is indicative of clinical judgment. T4L was ordered as an exclusive initial test for two patients (1%), one with unexplained reasons and the other with primary hypothyroidism. Requests for T4L should be indicated for suspected cases or for follow-up of central hypothyroidism, for the diagnosis of hyperthyroidism and for recent hyperthyroidism treatment (7, 8).

In the patients in this study, there was only one patient with a history of central hypothyroidism due to nonsecreting pituitary macroadenoma; a TSH and concomitant T4L test was requested. In patients with pituitary pathology, the measurement of free T4 should be an initial consideration

Table 2. *Distribution of evaluated variables according to necessity: the percentages and number of cases by category are described in the first two columns according to necessity; the last column describes percentages and number of cases according to the total number of patients.*

Variable	Necessary n (%)	Unnecessary n (%)	Total n (%)	P
Age, years. Me (IQR)*	61 (38-73)	61 (43-75)	61 (41-73)	0.710
Sex, female**	61 (54.5)	64 (53.8)	125 (54.1)	0.917
History of thyroid disease**	41 (36.6)	8 (6.7)	49 (21.2)	**<0.001** ⁺
Treatment with levothyroxine**	33 (29.5)	8 (6.7)	41 (17.7)	**<0.001** ⁺
Treatment with methimazole***	6 (5.4)	1 (0.8)	7 (3.0)	0.59
TSH request***	110 (98.2)	119 (100)	229 (99.1)	0.234
Abnormal TSH**	34 (32.1)	38 (31.9)	72 (41.4)	0.281
T4L request**	54 (48.2)	50 (42)	104 (45)	0.344
Abnormal T4L**	10 (18.5)	11 (22)	21 (20.1)	0.161
T3T request	5 (4.5)	10 (8.4)	15 (6.4)	0.225
Abnormal T3T	2 (40)	5 (50)	7 (46.6)	0.650
Use of drugs with the potential to alter protein binding	65 (58)	52 (59.7)	117 (50.6)	0.929

**Mann-Whitney U **Pearson's chi square ***Fisher's statistic ⁺Statistical significance p <0.05*

because TSH will be in the normal range or very slightly elevated despite a low T4 value (1, 9). The low rate of central hypothyroidism in this study is consistent with the literature, supporting that the vast majority of patients with hypothyroidism have a primary etiology.

The subgroup analysis performed to establish the initial profile of requested thyroid tests was focused on general medicine, internal medicine and psychiatry, which were the specialties that requested the most thyroid tests. While internists requested TSH as the most frequent initial test (61.4%), general practitioners requested TSH plus T4L more often (48.8%) and, although infrequent, had the highest number of joint requests for TSH, T4L and T3. Although requests for simultaneous TSH and T4L measurements can result in determining a clinical approach quicker, such requests do not guarantee that additional information will be obtained in support of international recommendations (4, 5, 9, 10). In turn, this increases costs (11, 12). Questioning and comprehensive approaches are the most valuable tools for establishing the pretest necessity of T4L combined with TSH requests, and this should be done in the face of a history of severe traumatic brain injury, postpartum hemorrhage, pituitary tumor, bitemporal hemianopsia, exposure to external cranial radiation or neurosurgery (7).

Different models of a one-step approach with initial TSH have been shown to capture and identify the vast majority of patients who require additional tests and to avoid cost overruns in health systems (12). Programs should be generated using laboratory values to make a decision tree for the complementary measurement of free T4 in case of obtaining low/suppressed TSH values, allowing the optimization of resources and length of hospital stay.

T3T was ordered for 15 patients (6.5%) and was always accompanied by TSH and T4L. For 11 patients, the requested T3L test was associated with high or normal TSH levels, supporting the previously reported findings in which the measurement of T3 is of no value for the diagnosis of primary hypothyroidism (13, 14) and should only be ordered under conditions of low or suppressed TSH levels or in clinical cases suggestive of hyperthyroidism or suspected euthyroid sick syndrome. Of the T3 tests requested, 12 of the 15 met necessity criteria for requesting TSH.

Table 3. *Profile of thyroid hormone tests requested by internal medicine, general medicine and psychiatry. T3 profile alone, T4L + T3, and TSH + T3 were not included because these profiles were not ordered by these specialties.*

Specialization	TSH (%)	T4L (%)	TSH + T4L (%)	TSH + T4L + T3T (%)
Internal Medicine	61.4	1.2	31.3	6.1
General Medicine	42.8	0	48.8	8.4
Psychiatry	61.5	0	38.5	0

Table 4. *TSH results according to necessity.*

TSH Result Ref Value (0.35-4.9)	Necessary (Category 1-4) N (%)	Unnecessary (Category 5-6) N (%)
High	27 (24.3)	33 (27.9)
Normal	76 (68.5)	78 (66.1)
Low	8 (7.2)	7 (6)
Total	111	118

In agreement with the necessity distribution in our study (Figure 3), some of the patients included in category 6 (38%) could be reclassified as necessary based on clinician criteria. Most thyroid tests reported in this study were normal in both categories. This opens the door and more strongly justifies the need for international guidelines that define criteria and clear indications for thyroid tests in hospitalized patients. It is important for the Colombian health auditing system that the justification of this request be reported in the clinical history; the lack of a supported reason lends itself to billing discrepancies and does not provide clear justification for a clinician ordering the test, constituting a limitation for the analysis of category 6.

TSH levels was normal in 67% of the patients. Of the tests that indicated high TSH levels, 36.5% were ordered with relevant criteria. The high proportion of elevated TSH levels in the unnecessary categories (63.5%) suggests to us that hypothyroidism encompasses multiple signs and symptoms and requires great clinical skill for an adequate diagnosis. This again supports the idea that a high proportion of patients in category 6 possibly had valid clinical criteria for requesting thyroid tests; however, for different reasons, the tests were not justified in the clinical history. In the case of low TSH levels, necessity was documented in for 65% of the requested tests, suggesting that the criteria established in the present study can provide adequate guidance when hyperthyroidism is suspected.

In 1995, an Italian study that evaluated 19181 outpatients and inpatients showed, at that time, that the most requested profiles were TSH + T4 + T3 (56%), followed by TSH + T4 L + free T3 (14%) and isolated TSH (12%). Normal values were found in 80.6% of T4 + T3 + TSH tests and 73.2% of T4 L + free T3 + TSH tests. Elevated TSH was more commonly found in inpatients than in outpatients (9.7 vs. 7.4%, p <0.001). In hospitalized patients, thyroid tests were requested for 20% of patients, and only one out of 14 had results indicating an alteration (15). Like the Italian study, in our study, the majority of requested TSH tests indicated normal values, indicating a need for optimizing the resources and requests in cases of a known history or presence of symptoms strongly suggesting thyroid etiology leading to patient hospitalization.

Of the tests classified as unnecessary (51.5%), 26.1% (31 cases) corresponded to category 5, and 73.9% (88 cases) corresponded to category 6. We believe that the degree of necessity could significantly improve if awareness is raised regarding providing an adequate record in the clinical history of the reason for the request. It is expected that in complex patients with multiple comorbidities, more relevant information needs to be provided in the clinical history, leading to the high omission rate for the justification for requested thyroid tests in medical records.

A total of 33.3% of the requested T4L tests in the necessary resulted in abnormal findings, while only 4.2% of the requested T4L tests in the unnecessary category resulted in abnormal findings, confirming that the request for thyroid tests in the absence of valid indications is of no use and will lead to a low probability of diagnostic information and thus constituting very cost-ineffective behavior. When evaluating unnecessary T4L test requests, in the majority of cases, there was a lack of justification in the clinical history (category 6) (Table 6).

Regarding requested TSH tests classified as unnecessary, most results were within normal limits or close to normal limits in category 5, while in category 6, 8% of TSH levels were below 0.1 or greater than 10 mIU/L, indicating a potential thyroid pathology. Of the TSH tests classified as necessary, 15% had results within limits of positivity, supporting that, given clear criteria for the test request, the pretest probability is higher and therefore cost-effective.

Of 10 patients who underwent anti-TPO complementary tests, one had normal TSH levels. If an initial test is normal, there is no recommendation for routinely measuring other additional thyroid studies, including anti-TPO. Such tests could be ordered to help confirm autoimmune etiology in patients with an established diagnosis of primary hypothy-

Table 5. *TSH and T4L distribution according to range and necessity.*

		Necessary (Cat 1 to 4) (%)	Unnecessary (Cat 5 and 6) (%)	Total
TSH ranges mUI/L	<0.1	5 (4.5)	3 (2.5)	8 (3.5)
	0.1 to 0.34	3 (2.7)	4 (3.4)	7 (3)
	0.35 to 4.9	76 (68.5)	78 (66.1)	154 (67.3)
	5 to 9.99	17 (15.3)	28 (23.8)	45 (19.7)
	10 to 20	3 (2.7)	3 (2.5)	6 (2.6)
	>20	7 (6.3)	2 (1.7)	9 (3.9)
Total TSH		111	118	229 (100%)
T4 ranges ng/dL	< 0.40	3 (5.2)	0	3 (2.9)
	0.41 – 0.70	7 (12.2)	2 (4.2.)	9 (8.7)
	0.71 – 1.47	38 (66.6)	45 (95.7)	83 (79.9)
	1.48 – 2	2 (3.5)	0	2 (1.9)
	> 2	7 (12.2)	0	7 (6.7)
Total T4 L		57	47	104 (100%)

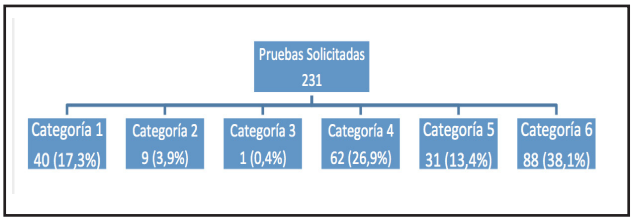

Figure 3. *Distribution of requested thyroid tests according to necessity.*

roidism, in patients with a subclinical hypothyroidism profile to help define the initiation of levothyroxine treatment (16) and in patients with goiter; however, TFTs will provide initial guidance to define a specific treatment.

We should be aware that TSH values may present age-related variations (17); obesity and subsequent hyperleptinemia is correlated with higher TSH levels (18), acute kidney disease is associated with low T3L levels, which improve once renal function improves (19), and the use of medications, especially amiodarone, can alter both the acute and chronic thyroid profile, inducing hypothyroidism in up to 20.8% of patients (20). The above should be considered by clinicians when interpreting requested thyroid test results.

One of the specific objectives of the present study was to establish which pathologies are associated with the most requested thyroid tests; however, it was not possible to determine this frequency with accuracy given that the heterogeneity of the diagnosis at admission did not follow a representative statistical mode.

Previous experience have shown that providing feedback to medical personnel allows optimizing and specifying the indications for TFT requests (6), emphasizing initial TSH as the best option; the initial combination of TSH, T4L, T3, anti TPO and anti-thyroglobulin tests were significantly reduced and maintained one year after raising awareness (2). Zhivko et al. reported the first systematic review that specifically evaluated the effectiveness of different interventions designed to reduce unnecessary thyroid tests (27 studies), including reducing the volume and changing the order pattern, improving adherence to the guidelines and reducing the cost of ordered thyroid tests; however, the variable heterogeneity of the evaluated evidence and possible biases in some of the studies evaluated did not allow for strong or specific conclusions. This opens the possibility for a future study in our population where the impact of providing feedback regarding criteria to the medical staff of our institution on thyroid test requests is evaluated.

Conclusions

As suggested in the available guidelines, TSH was the most requested test in the approach to hospitalized patients with suspected thyroid dysfunction.

The results from the majority of thyroid tests requested were normal, with similar percentages in both necessity categories.

Although 51.5% of the tests requested were classified as unnecessary according to the selection criteria of this study, the majority were classified as unnecessary because of the lack of justification in the clinical history, indicating the need for judicious recording of the reasons leading to the request of different diagnostic aids.

The present study reinforces the importance of clear criteria for requesting thyroid tests, and although we do not have definitive support guidelines, this study provides a tool that could be used to define thyroid tests in the medium term.

Table 6. *Unnecessary TSH and T4L tests distribution according to range.*

		Justification Without Indication (Cat 5) (%)	Without Justification in History (Cat 6) (%)	Total (%)
TSH ranges	<0.1	0	3 (3.4)	3 (2.5)
	0.1 to 0.34	1 (3.2)	3 (3.4)	4 (3.4)
	0.35 to 4.9	21 (67.8)	57 (65.6)	78 (66.1)
	5 to 9.99	8 (25.8)	20 (23)	28 (23.8)
	10 a 20	1 (3.2)	2 (2.3)	3 (2.5)
	>20	0	2 (2.3)	2 (1.7)
Total		31	87	118 (100%)
T4 ranges	< 0.40	0	0	0
	0.41 - 0.70	1 (11;1%)	1 (2.6%)	2 (4.2%)
	0.71 - 1.47	8 (88.9%)	37 (97.4%)	45 (95.7%)
	>1.48	0	0	0
Total		9	38	47 (100%)

Finally, we invite clinicians to reflect on cost-effectiveness when ordering thyroid tests and to take into account the impact generated in a health system when tests are ordered without clear justification.

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