

## Case Report

# Clinical, Laboratory, Ultrasound and FNAB Aspects of Subclinical Thyroid Diseases (Hypo and Hyperthyroidism)

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## Keywords

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## Introduction

The thyroid gland is the first gland to appear in the human embryo, exhibiting a highly organized structure and being able to synthesize and excrete its secretion products, the Thyroid Hormones (TH) triiodothyronine (T3) and thyroxine (T4), which are important for the development, growth and maintenance of the quality of life of human beings. The thyroid is one of the largest glands in the human body, weighing 15 to 20 grams during adult life, containing two lobes 2 to 2.5cm<sup>3</sup> in volume, and containing about 3 million follicles of various sizes [1].

The evaluation of thyroid dysfunctions is part of the investigation of many specialties. In general, thyroid function can be determined in a direct manner by palpation of the gland or using specific tests [2-5].

Non-thyroid diseases, pregnancy, various medications (especially amiodarone and lithium) and age may affect the extra-thyroid metabolism, the transport, absorption and/or action of TH, and may mimic dysfunction of this gland. The presence of anti-TSH or anti-TH antibodies results in abnormal findings [6-12]. The synthesis and secretory activities of TH are controlled or stimulated by thyrotropin hormone, which is produced by the thyrotrophic cells of the anterior pituitary. These activities also involve the presence of iodine and of a glycoprotein - thyroglobulin (Tg) - which is responsible for 70 to 80% of the entire protein content of the thyroid and is the site of TH synthesis. Tg levels increase in the individuals by accompanying the increase in gland volume (goiter) [13,14].

Hashimoto's thyroiditis is associated with the presence of anti-thyroperoxidase and/or anti-thyroglobulin titers and is accompanied by diffuse or nodular goiter and/or by heterogeneity of the thyroid parenchyma, being the main cause of acquired hypothyroidism [15-18].

Hypothyroidism is the syndrome induced by TH deficiency and by increased levels of TSH and of thyroid antibody titers (anti-

thyroperoxidase and/or anti-thyroglobulin) and is associated with Hashimoto's thyroiditis [19,20].

Hyperthyroidism is the syndrome caused by excess TH, suppression of TSH, increased levels of antithyroid antibodies (anti-thyroperoxidase, anti-thyroglobulin and anti-TSH receptor) and is associated with Graves' disease [21].

Subclinical thyroid dysfunctions are characterized by normal TH levels and altered (increased or decreased) TSH levels. They are highly prevalent in the general population and their significance and the need for drug treatment are topics of debate in clinical practice.

The increasing number of prospective population and meta-analysis studies about the effect of subclinical disease on the cardiovascular system and on life expectancy has led to a new consensus regarding the indications of treatment for these two clinical entities.

## Case Presentation

The study was conducted on 145 patients (27 men and 118 women) with subclinical hypothyroidism (TSH value > 4.5μIU/L and normal free T4 and T3 values) and 45 patients (8 men and 37 women) with subclinical hyperthyroidism (TSH value < 0.1μIU/L and normal free T4 and T3 values) (Table 1). Age ranged from 23 to 79 years (mean: 50.18 years) for hypothyroid men and from 20 to 84 years (mean: 41.61 years) for hypothyroid women, and from 54 to 86 years (mean: 70.75 years) for hyperthyroid men and from 27 to 89 years (mean: 62.37 years) for hyperthyroid women (Table 2).

The following laboratory exams were carried out by electrochemiluminescence: TSH (thyrotropic hormone- RV: 0.27-4.5mIU/L; free T4 (free thyroxine- RV: 0.9-1.9ng/dl), free T3 (free triiodothyronine- RV: 2.0-4.4ng/d), thyroglobulin (Tg - RV: 1.4-78ng/ml)), anti-TPO antibody (anti-thyroperoxidase- RV: <34IU/ml), anti-thyroglobulin antibody (Anti Tg- RV:<115UI/ml), and anti-TSH receptor antibody (TRAB- RV: <1.75UI/ml) (Table 3).

Ultrasound examination was applied to the patients with palpable or suspected thyroid nodules found during routine physical exam and in an 8000 EX imaging system (Samsung Medson Co, Seoul, Korea). Lesions were classified as solid or cystic or complex nodules.

Ultrasound examination was also used to guide FNAB of nodules larger than 10mm and the aspirated material was stained with hematoxylin-eosin and submitted to histopathology examination.

## Results

Mean TSH values were 7.73mIU/L and 5.72mIU/L, 0.115mIU/L and 0.081mIU/L for hypothyroid and hyperthyroid men and women, respectively.

**Table 1:** Distribution of hormone levels and other parameters studied.

Hypothyroidism											
Females						Males					
TSH	T4L	T3L	Tg	Anti TPO	Anti-Tg	TSH	T4L	T3L	Tg	Anti TPO	Anti-Tg
5.72	1.11	2.97	50.14	197.05	140.01	7.73	0.96	2.88	27.13	93	101.29

TSH= mIU/L; T4L=ng/dl; T3L= ng/dl; Tg (thyroglobulin) = ng/dl; Anti-TPO= IU/ml; Anti-Tg= IU/ml.

**Table 2:** Distribution of hormone levels and other parameters studied.

Hypothyroidism											
Females						Males					
TSH	T4L	T3L	Tg	Anti TPO	Anti-Tg	TSH	T4L	T3L	Tg	Anti TPO	Anti-Tg
0.08	1.27	3.19	50.14	112.54	78.09	0.115	1.47	2.71	29	54	161.25

TSH= mIU/L; T4L=ng/dl; T3L= ng/dl; Tg (thyroglobulin) = ng/dl; Anti-TPO= IU/ml; Anti-Tg= IU/ml.

Free T4 values were 0.96ng/dl and 1.11ng/dl; 1.47ng/dl and 1.27ng/dl for hypothyroid and hyperthyroid men and women, respectively.

Free T3 values were 2.88ng/dl and 2.97ng/dl; 2.71ng/dl and 3.19ng/dl for hypothyroid and hyperthyroid men and women, respectively.

Tg values were 27.13ng/dl, 50.14ng/dl; 29ng/dl and 112.54ng/dl for hypothyroid and hyperthyroid men and women, respectively.

Anti-TPO values were 93 IU/ml, 197.05 IU/ml, 54 IU/ml, and 74.78 IU/ml for hypothyroid and hyperthyroid men and women, respectively. Anti-Tg values were 101.29IU/ml, 140.01IU/ml, 161.25IU/ml, and 78.09/ml for hypothyroid and hyperthyroid men and women, respectively. TRAB values were 0.82IU/ml, 0.66IU/ml; 4.34 IU/ml and 4.55IU/ml for hypothyroid and hyperthyroid men and women, respectively.

The following histological results were obtained for hypothyroid patients: 2 and 9 cases of a single solid nodule, 2 and 14 cases of multiple solid nodules, 4 and 7 cases of simple cysts, no case and 7 cases of solid nodules and cysts in the same gland, 15 and 36 cases of diffuse goiter, no case and 1 case of a micronodular gland, 1 case and no case of pseudonodules, and 2 and no cases of reduced glands among male and female patients, respectively.

Among hyperthyroid patients, the results were: 1 and 5 cases of a single solid nodule, 1 and 15 cases of multiple solid nodules, 2 and 1 cases of simple cysts, none and 3 concomitantly solid and cystic nodules, and none and 1 case of diffuse goiter among hyperthyroid men and women, respectively. No malignant lesion was detected by cytopathological examination.

## Discussion

Altered TSH levels in the presence of normal TH levels characterize the subclinical thyroid dysfunctions, which may affect up to 20% of the adult population studied. Despite this high prevalence in the population and the increased diagnostic frequency, the significance of this condition and the need for its treatment continue to be controversial in clinical practice [22].

Among older people (more than 65 years of age), TSH values undergo a physiological elevation, the recommendation being to use the reference values for each age range [22].

**Table 3:** Distribution of TRAB (TSH receptor stimulating antibody).

TRAB			
Hypothyroidism		Hyperthyroidism	
Females	Males	Females	Males
0.66	0.82	4.55	4.34

TRAB= IU/ml.

Hypothyroidism is a highly prevalent condition regardless of the criterion used to define it. In a study conducted in England, 7.5% of the women and 2.8% of the men had TSH levels > 6mIU/L, and in an American study conducted in Colorado on 25,862 subjects, about 11.7% of the participants showed abnormal serum TSH. In Brazil, a study conducted in Rio de Janeiro using a cut-off value of TSH >4mIU/L detected altered values or treatment with levothyroxine in 12.3% of the 1298 female participants [4].

Subclinical hypothyroidism (scHypo) commonly occurs in the population, with a higher prevalence and incidence than subclinical hyperthyroidism (scHyper). The condition is usually asymptomatic and, when symptoms are present, the more frequent ones are dry skin, impaired memory, fatigue, muscle weakness, and intestinal constipation. However, there are no reports of worse quality of life, cognitive changes, depression or anxiety, even among older persons [22].

Thyroid hormones have positive inotropic and chronotropic effects, and similar effects have been reported among patients with scHyper [22-24]. An increasing number of studies have associated persistent scHyper with worsening of quality of life, cognitive changes, a higher risk of osteoporosis and fractures, as well as an increase in cardiovascular and mortality risk [23]. A risk association between scHyper and atrial fibrillation has been observed in older patients with TSH <0.44μIU/L. It has also been confirmed that endogenous scHyper, with TSH levels of 0.1μIU/L or less, is more frequently associated with the risk of atrial fibrillation [23].

The prevalence of scHyper varies according to the population studied, iodine content in the diet, and patient sex and age. It is higher among older and black women and in iron-deficient population, ranging from 1 to 3.2%, but in general being lower than 1%. In regions considered to be in transition in terms of dietary iodine content, the prevalence of scHyper is high, with an estimated prevalence of 10% in the general population, varying according to sex, age, ethnicity, and dietary iodine content. No treatment has been established for either

scHypo or scHyper, with controversy persisting about therapy.

A recent meta-analysis has shown a significant association between these conditions and an increased risk of coronary artery events and mortality due to any cause or of cardiovascular cause after adjustment of correction factors. These data have been considered compelling and definitive about the persistent impact of scHyper on cardiovascular risk, especially in the presence of TSH levels <0.1mIU/L [23-25]. scHyper has also been associated with greater bone loss during menopause, with a higher risk of bone fractures and also with changes in cognitive function and mood and with anxiety, depression and dementia [24].

In the present study, women were younger and also older ones were younger than men. Men showed worse TSH, T4L, T3L, Anti Tg and TRAB values, a fact possibly suggesting that subclinical thyroid disease is more marked and more compromising for this gland among males. No other systemic involvement was observed in the patients studied, except for the presence of diffuse or nodular goiter (single or multiple), with a predominance of this finding among women.

## Conclusion

In the present study women were younger and also older ones, and in media age were younger than men. Men were the less number in this studied and showed the worst TSH, T4L, T3L, Anti Tg and TRAB values, when compared with women. This fact suggests that thyroid diseases are less common in men, but when subclinical thyroid disease happens, it is more marked and more compromising for this gland among them. No other systemic involvement was observed in the patients studied, except for the presence of diffuse or nodular goiter (single or multiple), with a predominance of this finding among women.

## References

- Bianco AC. Fisiologia da glândula tireoide. In: Rosa JC, Romão LA (eds) *Glândula Tireoide: Funções e Disfunções- Diagnóstico e Tratamento*. Second edition. Lemos, São Paulo, Brazil. 2001; 33-46.
- Lamberger BA. Endemic goiter- iodine deficiency disorders. 1991; 23: 367-372.
- Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F. The spectrum of thyroid disease in a community the Whickham Survey. *Clin Endocrinol (Oxf)*. 1977; 7: 481-493.
- Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Arch Intern Med*. 2000; 160: 526-593.
- Alves MLD, Gabarra MHC. Evaluation of Thyroid Function in a Group of Recently Diagnosed Patients with Thyroid Diseases Followed up at the Endocrinology Outpatient Clinic of University of Ribeirão Preto (UNAERP)- São Paulo Brazil. *J Endocrinol*. 2017; 1: 000102.
- Gurnell M, Halsall DJ, Chatterine VK. What should be done when thyroid function tests do not make sense? *Clin Endocrinol*. 2007; 74: 673-678.
- Dufour DR. Laboratory tests of thyroid function: uses and limitations. *Endocrinol Metab Clin North Am*. 2007; 36: 579-594.
- Tahboub R, Arafat BM. Sex steroids and the thyroid. *Best Pract Res Clin Endocrinol Metab*. 2009; 23: 769-780.
- Danzi S, Klein I. Amiodarone- induced thyroid dysfunction. *J Intensive Care Med*. 2015; 30: 179-185.
- Lazarus JH. The effects of lithium therapy on thyroid and thyrotropin-realizing hormone. *Thyroid*. 2009; 8: 909-913.
- Faggiano A, Del Prete M, Marciello F, Marotta V, Ramundo V, Colao A. Thyroid diseases in elderly. *Minerva Endocrinol*. 2011; 36: 211-231.
- Kwok JS, Chan JH, Chan MH. Biotin interference on TSH and free thyroid hormone measurement. *Pathology*. 2012; 44: 278-280.
- Salvatore D, Davies TE, Schlumberger MJ, Ian D Hay. Thyroid physiology and diagnostic evaluation of patients with thyroid disorders. 2011; 327-337.
- Sakata S, Matsuda M, Ogawa T, Hiroshi T, Ikuo M, Sarui H, et al. Prevalence of thyroid hormone autoantibodies in healthy subjects. *Clin Endocrinol*. 1994; 41: 365-370.
- Gharib H, Tuttle RM, Baskin HJ, Fish LH, Singer PA, et al. Subclinical thyroid dysfunction: a joint statement on management from the American Thyroid Association of Clinical Endocrinologists, the American Thyroid Association and Endocrine Society. *J Clin Endocrinol Metab*. 2005; 90: 581-585.
- Graf H, Carvalho GA. Fatores Interferentes na interpretação de dosagens laboratoriais no diagnóstico do hiper e hipotireoidismo. *Arq Bras Endocrinol Metab*. 2002; 46: 51-64.
- Brenta G, Vaisman M, Sgarbi JA, Liliana MB, de Andrada NC, Bravo PP, et al. Clinical practice guidelines for management of hypothyroidism. 2013. *Arq Bras Endocrinol Metab*. 2013; 57: 265-291.
- Okosiene O, Gilbert J, Abrahan, P, Boelaert K, Dayan C, Gurnell M, et al. Management of primary hypothyroidism: statement by British Thyroid Association Executive Committee. *Clin Endocrinol*. 2016; 84: 799-808.
- Sweeny LB, Stewart C, Gaitonde DY. Thyroiditis: an integrated approach. *Am Fam Physician*. 2014; 90: 389-396.
- Sichieri R, Baima J, Henriques J, Vasconcellos M, Marante T, Kumagai S, et al. Prevalence of thyroid disease and positive antithyroperoxidase among 1500 women 35 year old: a population based survey in the city of Rio de Janeiro, Brazil. 2005.
- Bahn Chair RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guideline of The American Thyroid Association and American Association of Clinical Endocrinologists. *Endocr Pract*. 2011; 17: 456-520.
- Sgarb JA. Doenças Tireoidianas Subclínicas. In: *Endocrinologia Princípios e Prática*. 2ª edição. Saad MJA, Maciel RMB, Mendonça BB. 449-458.
- Romaldini JH, Sgarb JA, Farah CS. Subclinical thyroid 44 disease: subclinical hypothyroidism and hyperthyroidism. *Arq Bras Endocrinol Metab*. 2004; 48: 147-158.
- Valdiveoloo, T, Donnan PT, Cochrane L, Leese GP. The thyroid epidemiology, audit, and research study (TEARS): morbidity in patients with endogenous subclinical hyperthyroidism. *J Clin Endocrinol Metab*. 2011; 96: 1344-1351.
- Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. *Endocrine Review*. 2008; 29: 76-131.