

# Evaluation of Thyroid Function in a Group of Recently Diagnosed Patients with Thyroid Diseases Followed up at the Endocrinology Outpatient Clinic of the University of Ribeirão Preto (Unaerp) - São Paulo, Brazil

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## Case Report

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## Abstract

**Introduction:** The determination of thyroid dysfunction is part of the clinical investigation in different medical specialties. Non-thyroid disorders, certain medications and age may affect the hormonal results. The presence of anti-TSH or anti-thyroid hormone antibodies may result in abnormal findings.

**Objective:** To evaluate thyroid function parameters in a group of subjects with recently diagnosed and untreated thyroid disease taking no medication.

**Cases:** The study was conducted on 301 patients of both sexes, 275 of them non-pregnant women (91.3%) aged 18 to 87 years and 26 of them men (8.7%) aged 21 to 85 years. The subjects were compared to 166 control patients with no thyroid disorders, 123 of them women (75.3%) aged 18 to 81 years and 43 of them men (24.7%) aged 19 to 66 years. The patients were divided into the following groups: Group A-Control Patients; Group B-Subclinical Hypothyroidism; Group C-Clinical Hypothyroidism; Group D-Subclinical Hyperthyroidism; Group E-Clinical Hyperthyroidism; Group F-Chronic Thyroiditis; Group G-Goiter; Group H-Papilliferous Carcinoma; Group I-Previous Hyperthyroidism.

**Results:** The female sex was preponderant in all groups, with no males occurring in the Clinical Hyperthyroidism, Papilliferous Carcinoma or Previous Hyperthyroidism groups. Patients with Subclinical Hyperthyroidism and Goiter belonged to significantly older age ranges. Mean TSH values were higher in the Clinical and Subclinical Hyperthyroidism Groups. Free T4 and T3 levels were significantly lower in Clinical Hypothyroidism and significantly higher in Clinical Hyperthyroidism. Mean Thyroglobulin levels were significantly higher in the Goiter Group and mean Anti-Thyroglobulin antibody (Anti-Tg) and Anti-Thyroperoxidase (Anti-TPO) levels were significantly higher in the Chronic Thyroiditis

group. The Anti-TSH receptor (TRAB) antibody was significantly higher in the Clinical Hyperthyroidism Group and the finding of Toxic Multinodular Goiter predominated in the Subclinical Hyperthyroidism Group.

**Conclusion:** Autoimmune thyroid disorders predominated among females and in the less advanced age ranges and structural thyroid disorders and high level of thyroglobulin predominated in the more advanced age ranges.

**Keywords:** Thyroid dysfunctions; Thyroiditis; Graves' disease; T3; T4; TSH

## Introduction

The thyroid gland is the first endocrine gland arising in the human embryo, presenting a highly organized structure and able to synthesize and store its secretion products, i.e., the thyroid hormones (TH) triiodothyronine (T3) and thyroxine (T4), important for the development, growth and maintenance of the quality of life of human beings. Checking for thyroid dysfunctions is part of the clinical investigation in various medical specialties. In general, thyroid function tests can be interpreted in a simple and direct manner [1,2]. Non-thyroid diseases, pregnancy [3], some medications (mainly amiodarone and lithium) [4-6] and age [7] can affect extra-thyroid metabolism and the transport, absorption and/or action of thyroid hormones, mimicking dysfunction of this gland [8-11]. The presence of anti-TSH or anti-TH antibodies may result in abnormal findings [12].

The synthetic and secretory activity of the thyroid is basically stimulated or controlled by pituitary thyrotropin (TSH) and involves the presence of iodine and thyroglobulin (Tg) which is responsible for 70 to 80% of the entire protein content of this gland. Thyroglobulin (Tg) is a glycoprotein whose levels are increased in almost patients with differentiated thyroid cancer, subacute thyroiditis and endemic goiter, representing a marker of thyroid disease. The involvement of the thyroid by agents that induce a granulomatous and nonspecific inflammatory reaction causes thyroiditis, which is classified as acute, subacute and chronic. Hashimoto's thyroiditis is associated with an increase in antithyroperoxidase (anti-TPO) and/or anti-thyroglobulin (anti-Tg) antibody titers. It is characterized by a diffuse enlargement of the thyroid and is the main cause of acquired hypothyroidism. Hyperthyroidism is a syndrome due to increased TH synthesis and secretion by the thyroid, with Graves' disease (autoimmune) being the more frequent form which courses with elevated titers of anti-TPO, anti-Tg and TRAB (anti-TSH receptor antibody), accompanying or not to the development of

ophthalmopathy. Cancer of the thyroid is the most frequent among endocrine tumors, with the papilliferous tumor representing up to 88.5% of cases.

## Objective

To evaluate thyroid function parameters in a group of patients with recently diagnosed and still untreated thyroid disease, taking no medication and followed up at the Endocrinology outpatient clinic of the University of Ribeirão Preto- UNAERP, São Paulo, Brazil.

## Cases and Methods

The study was conducted on 306 patients of both sexes, not taking amiodarone, lithium, biotin and corticosteroid, 279 of them non-pregnant women (91.3%) ranging in age from 18 to 87 years and 27 of them men (8.7%) ranging in age from 21 to 85 years. The subjects were compared to 167 control patients (with no thyroid disorder diagnosed upon investigation and followed up at this service due to another type of endocrine disease- dyslipidemia, obesity, pre bariatric surgery- and not taking any medicine), 123 of them women (75.3%) ranging in age from 18 to 81 years and 44 of them men (24.7%) ranging in age from 19 to 66 years. The study was approved by the Ethics Committee of UNAERP ("Plataforma Brasil" Protocol: 27031207) and all patients gave written informed consent to participate. All subjects were submitted to the determination of TSH, Free T4, Free T3, Tg, Anti-TPO, Anti-Tg, and TRAB, to ultrasound (US) examination in cases of diffuse or nodular goiter, and to Fine Needle Aspiration Biopsy (FNAB) in cases of nodular disease. No patient with Graves' disease had clinical ophthalmopathy. All measurements were made by electrochemoluminescence using the following normal reference values for adults: 0.27 to 4.5  $\mu$ U/ml TSH, 0.8 to 1.9 ng/dl Free T4, 2.0 to 4.4 ng/ml Free T3, 1.4 to 78 ng/ml Thyroglobulin, < 34 IU/ml Anti-TPO, <116 IU/ml Anti-Tg, and <1.75 IU/L TRAB [7,8]. US examination was performed using a Samsung-Medison 8000 EX apparatus

(Samsung Medison Co., Seoul, Korea). FNAB was performed on an ambulatory basis and the material obtained was examined after staining with hematoxylin-eosin.

### The patients were divided into 9 groups according to their diagnosis

Group A-Control Patients

Group B- Subclinical Hypothyroidism (Elevated Tsh - Normal T3 and T4) [13]

Group C-Clinical Hypothyroidism [14-16]

Group D-Subclinical Hyperthyroidism (Reduced Tsh, Normal T3 and T4) [13]

Group E-Clinical Hyperthyroidism [17]

Group F-Chronic Thyroiditis [18]

Group G-Goiter [19,20]

Group H-Carcinoma (Papilliferous) [20]

Group I-Previous Hyperthyroidism [13,17]

### Results

The results obtained in the present study were analyzed statistically by the two-tailed MANN-WHITNEY test and by the DUNNETT test and are listed in (Tables 1-3). The female sex was preponderant in all groups, with no males occurring in the Clinical Hyperthyroidism, Carcinoma (Papilliferous) or Previous Hyperthyroidism groups. Patients with Subclinical Hyperthyroidism and Goiter belonged to significantly older age ranges compared to the remaining groups ( $p < 0.0001$ ). Mean TSH values were higher in the Clinical Hypothyroidism and Chronic Thyroiditis groups and were lower in the Clinical

and Subclinical Hyperthyroidism group. Free T4 and Free T3 values were significantly lower in the Clinical Hypothyroidism group and significantly higher in the Clinical Hyperthyroidism group ( $p < 0.0001$ ). Mean Tg values were significantly higher among patients with Goiter and Anti-TG and Anti-TPO values were significantly higher among patients with Chronic Thyroiditis (evaluations performed before FNAB) ( $p < 0.0001$ ). TRAB levels were significantly higher in the Clinical Hyperthyroidism group ( $p < 0.0001$ ). The detection of Toxic Multinodular Goiter predominated in the Subclinical Hyperthyroidism group.

	M	F	M + F
Group	1	2	Total
A	44	123	167
B	2	20	22
C	1	7	8
D	5	16	21
E		8	8
F	9	70	79
G	9	149	159
H		4	4
I		5	5
Total	71	402	473

Table 1: Characterization of the groups studied according to frequency by sex.

M = Male; F - Female

Group	Sex	N	Minimum	Maximum	Mean	Sd
A	1	44	19	66	38.8	12.6
	2	123	18	81	39.3	14.36
B	1	2	28	73	50.5	31.82
	2	20	20	78	50.5	14.84
C	1	1	41	41	41	-
	2	7	20	84	39.7	25.26
D	1	5	54	85	69.6	14.43
	2	16	29	79	56.6	18.41
E	1	-	-	-	-	-
	2	8	21	65	41.3	17.29
F	1	9	21	72	47.6	16.3

	2	70	18	87	43.4	15.7
G	1	10	44	70	55.6	10.2
	2	149	18	84	54.2	15.3
H	1	-	-	-	-	-
	2	4	23	63	42.5	16.4
I	1	-	-	-	-	-
	2	5	46	82	55,6	15,1

Table 2: Descriptive Age Data: N. Of Samples, Minimum Value, Maximum Value, Mean And Standard Deviation.

Mean Values Of The Indicators Per Group								
Groups	Mean Age (Years)	Tsh ( $\mu$ iu/MI)	Free T4 (Ng/MI)	Free T3 (Pg/MI)	Tg (Ng/MI)	Antitg (Iu/MI)	Antitpo (Iu/MI)	Trab (Iu/L)
A	39.2	1.2	1.11	3.17	33.33	10.74	13.01	0.42
B	50.5	1.9	1.11	3.24	21.63	20.14	7.99	0.47
C	40,5	30.8	0.79	2.47	82.8	89.58	98.97	0.34
D	59.7	0.2	1.37	3.12	60.14	74.17	53.01	1.46
E	41.3	0	3.49	8.83	44.18	192.99	172.3	9.02
F	43.9	6.2	1.06	2.93	38.47	294.09	223.81	0.59
G	54.3	2.3	1.11	2.82	46.58	27.11	22.09	0.42
H	42.5	6.5	1.39	3.58	5.62	7.21	8.71	0.3
I	55.6	2.2	1.06	2.77	29.85	216.38	165.91	0.47
General	46.5	3.4	1.15	3.08	39.85	74.19	58.88	0.65

Table 3: Mean Values of the Indicators per Group.

## Discussion

The female sex predominated in all groups including the Control Group, indicating that endocrine diseases are preponderant among women or that women seek the help of endocrinologists more frequently. The Clinical Hypothyroidism, Subclinical Hyperthyroidism, Goiter and Previous Hyperthyroidism groups involved the older age ranges, confirming the higher prevalence of these diseases with increasing age. A younger age range predominated in Clinical Hyperthyroidism, a characteristic of autoimmune diseases. The Clinical Hyperthyroidism, Carcinoma (Papilliferous) and Previous Hyperthyroidism groups did not contain any males, indicating the higher prevalence of these endocrine diseases among females. TSH, Free T4 and Free T3 were altered in the Clinical Hypothyroidism (higher TSH and lower T3 and T4) and Clinical Hyperthyroidism (lower TSH and higher T3 and T4) groups, clearly indicating the occurrence of thyroid dysfunction in these diseases with repercussions on pituitary control. The Anti-Thyroid Antibody (Anti-Tg and Anti TPO) findings were significant in the Thyroiditis, Goiter and Previous Hyperthyroidism

groups, diseases that course with changes in the thyroid parenchyma. In the Clinical Hyperthyroidism Group – a thyroid disease related to autoimmunity, Anti-TPO, Anti-TG and TRAB were positive, the last one exclusive and a marker of this endocrine disease. There was a small, nonsignificant positivity for TRAB in the Subclinical Hyperthyroidism Group, possibly indicating the presence of patients with Pre-Graves' disease in this group. Thyroglobulin values were higher in the Goiter Group, possibly indicating structural thyroid changes since there was no interference of aggression to the thyroid parenchyma by the execution of the FNAB procedure before its collection. The Carcinoma (Papilliferous) Group did not show any specific laboratory changes, with its diagnosis being exclusively based on FNAB findings and confirmed by histopathological analysis. During old age, accompanying the regression that occurs in other parts of organism, the volume of the thyroid may reduced, with an increase in connective tissue and a consequent multinodular aspect. Multinodular goiter was more found in our old patients.

## Conclusion

The laboratory data obtained in the present study showed that female sex and less advanced age ranges were typical of autoimmune thyroid disease, that structural thyroid diseases and high levels of Thyroglobulin predominated among the more advanced age ranges and that the patients benefited from the evaluation of thyroid function by means of the tests presented, with increased accuracy of diagnosis and treatment of the various thyroid diseases.

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