EVOLUTION OF THYROID FUNCTION IN OLDER PATIENTS WITH HASHIMOTO'S THYROIDITIS AND RELATED CONDITIONS – PART 1

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Abstract. Aim of the study was to establish if there are differences in the evolution of thyroid function in older patients with Hashimoto's thyroiditis and related conditions as compared to younger counterparts. We investigated a total of 4.668 patients, 2.034 being diagnosed with Hashimoto's thyroiditis (HT). Thyroid function was assessed by thyroid hormone free thyroxin (FT4) and by hypophyseal/pituitary thyroid stimulating hormone (TSH). Patients with Hashimoto's thyroiditis had a higher prevalence of euthyroidism (46.51%) than with hypothyroidism (40.86%). In older patients the prevalence of euthryoidism (45.59%) and hypothyroidism (45.8%) was the same at the time of admission. Patients with hyper-AGT (T-ATG) thyroiditis were even more euthyroid (71.26% vs. 22.47% hypothyroid) than those with Hashimoto's (classical) thyroiditis; p<0.01. In older patients the prevalence is different; more hypothyroidism: 56.25% vs. 35.41%, p<0.01. Only 4% of patients with euthyroidism and T-ATG become hypothyroid. In older patients the evolutional pattern is preserved: only 2% (NS). After more than 20 years of observation, in cases of Hashimoto's thyroiditis, respectively 5 years, in those with hyper-ATG thyroiditis, no changes in thyroid function are observed. This suggests that most patients with euthyroidism will remain euthyroid all their lives. The older patients have the same pattern. Patients with T-ATG and hyperthyroidism (6.3%) appeared to be associated with Graves-Basedow's disease in much lower prevalence than the phenomenon observed in TH: only 50% had TRAB positive. The older patients with this association reach a prevalence of 8.33%, no statistical difference. Almost all patients with hyperthyroidism became normothyroid under the antithyroid treatment. In 5 years only 5 relapses were registered. In older patients hyperthyroidism was under control, no relapse. About 3% of the hyperthyroid patients became spontaneous hypothyroid. Older patients with Hashimoto's thyroiditis and related conditions demonstrate some specific patterns of evolution if thyroid function that warrant further investigation.
Keywords: autoimmune thyroiditis, Hashimoto's thyroiditis, hypothyroidism, hyperthyroidism, older patients

Rezumat. Scopul studiului a fost de a stabili dacă există diferenţe în evoluţia funcţiei tiroidiene la pacienţii mai în vârstă cu tiroidita Hashimoto şi afecţiunile asociate, în comparaţie cu omologii mai tineri. Am investigat un total de 4.668 de pacienţi, 2.034 fiind diagnosticaţi cu tiroidita Hashimoto (HT). Funcţia tiroidiană a fost evaluată prin tiroxina liberă de hormoni tiroidieni (FT4) şi prin hormonul de stimulare a tiroidei hipofizar/hipofizar (TSH). Pacienţii cu tiroidita Hashimoto au avut o prevalenţă mai mare a eutiroidismului (46,51%) decât cu hipotiroidism (40,86%). La pacienţii vârstnici prevalenţa eutiroidismului (45,59%) şi a hipotiroidismului (45,8%) a fost aceeaşi la momentul internării. Pacienţii cu tiroidită hiper-AGT (T-ATG) au fost chiar mai eutiroidieni (71,26% vs 22,47% hipotiroidă) decât cei cu tiroidită Hashimoto (clasică); p<0,01. La pacienţii în vârstă prevalenţa este diferită; mai mult hipotiroidism: 56,25% vs 35,41%, p<0,01. Doar 4% dintre pacienţii cu eutiroidism şi T-ATG devin hipotiroidieni. La pacienţii mai în vârstă se păstrează modelul evolutiv: doar 2% (NS). Dupa mai bine de 18 ani de observatie, in cazurile de tiroidita Hashimoto, respectiv 5 ani, la cei cu tiroidita hiper-ATG, nu se observa modificari ale functiei tiroidiene. Acest lucru sugerează că majoritatea pacienţilor cu eutiroidism vor rămâne eutiroidieni toată viaţa. Pacienţii mai în vârstă au acelaşi model. Pacienţii cu T-ATG şi hipertiroidism (6,3%) au părut a fi asociaţi cu boala Graves-Basedow cu o prevalenţă mult mai mică decât fenomenul observat în TH: doar 50% au avut TRAB pozitiv. Pacienţii mai în vârstă cu această asociere ajung la o prevalenţă de 8,33%, fără diferenţă statistică. Aproape toţi pacienţii cu hipertiroidism au devenit normotiroidieni sub tratamentul antitiroidian. În 5 ani s-au înregistrat doar 5 recidive. La pacienţii vârstnici hipertiroidismul a fost sub control, fără recidivă. Aproximativ 3% dintre pacienţii hipertiroidieni au devenit hipotiroidieni spontan. Pacienţii mai în vârstă cu tiroidita Hashimoto şi afecţiunile asociate demonstrează unele modele specifice de evoluţie dacă funcţia tiroidiană necesită investigaţii suplimentare.
Cuvinte cheie: tiroidita autoimuna, tiroidita Hashimoto, hipotiroidism, hipertiroidism, pacienţi vârstnici

DEFINITIONS

A. Syndrome vs. disease

In endocrinology, the modification of the function of a certain hormone/gland, evaluated according to the admitted models, does not represent a disease, but it represents a syndrome. In terms of function, any kind of endocrine secretion can have only three expressions: within the limits of normality, called eu-….-ism, lower than normal, called hypo-….-ism, or higher than normal, called hyper-… -ism.

For example, when the level of the cortisol hormone is higher than normal, the syndrome is called "hypercorticism" or "hypercortisolism". If it is smaller, then it is either "hypocorticism" or "hypocortisolism". When we want to refer to blood concentrations, the suffix "... emia" is used. Hyperprolactinemia, for example, is not a disease and is not a syndrome, too. It is only an observation that there is more prolactin in the blood. From a syndromic point of view, it would be hyperprolactinism, an expression not yet in use.

Therefore, related to the thyroid, there is no disease called hyperthyroidism, as there is no disease called hypothyroidism. These are syndromes. A thyroid disease can develop with both hyperthyroidism and hypothyroidism, obviously in its different observation moments, as we will present in the current analysis. For example, although Graves Basedow's disease is known to occur most often with hyperthyroidism, there are cases of Graves-Basedow's disease with spontaneous (spontaneous, i.e., non-therapeutic) hypothyroidism. Although Hashimoto's thyroiditis has been described (and is) related to the syndromic hypothyroidism, there are quite a few cases of Hashimoto's thyroiditis with spontaneous hyperthyroidism.

Related to the syndrome, there is a "subclinical hyperthyroidism", as well as there is a "subclinical hypothyroidism". However, in the current stage of medicine development, even the "clinical" syndrome does not express something "clinical", but also a biological analysis. When hypothyroidism is clinical, the notion refers to the FT4 level and not to the clinical aspect of the patient.

B. On thyroiditis

Immune thyroiditis is characterized by thyroid inflammation associated with specific immune mechanisms. Defining thyroiditis as Hashimoto's thyroiditis has gone through a historical process.

Initially, Hakaru Hashimoto (1881-1934) described in 1912 [1] a form of thyroid disease with thyromegaly with follicular inflammation and hypothyroidism different from the hypothyroidism with thyroid atrophy, then called "myxedema" or "thyroiditis of Ord" (Ord's thyroiditis). William Miller Ord (1834-1902) described the thyroid atrophy with thyroid inflammation as early as 1877. Subsequently, in our times, the pathogenesis of the thyroid injury was recognized as immunological and thus received the name of "lymphocytic", "chronical", and/or "autoimmune".

Under the clinical spectrum, it has been observed that patients with thyroiditis may also be normothyroid (euthyroidism), not necessarily hypothyroid, as initially described by Hashimoto.

Investigating the pathogenesis of this disease, it was observed that it is generated by an antibody called "antimicrosomal", because it affects certain intracellular organisms of the thyroid, i.e. microsomes. To the "antimicrosomal" antibody was then discovered the antigen: thyroperoxydase. Thus, the name of antimicrosomal antibody has been changed, the antibody becoming "anti-thyroperoxydase" (ATPO). Then, Ord's thyroiditis was shown to occur through the same antibodies.

Thus, Hashimoto's thyroiditis became from thyroiditis with myxedema and thyromegaly that thyroiditis with anti-thyroperoxydase antibodies**.** In this chronic and lymphocytic inflammation of the thyroid, the autoantibodies behave in a specific way, generating a specific immune mechanism. This mechanism was describes as *antibody dependent cellular cytotoxicity* (ADCC) [2]. Thus, in defining the disease, the size of the thyroid does not appear, nor its functionality.

The existence of a strictly individualized immune mechanism makes the broader notion of "thyroid immune/autoimmune disease" meaningless. In this broad context, some believe that Graves-Basedow's disease, Hashimoto's thyroiditis, postpartum thyroiditis or other silent forms of immune thyroid disease represent a single disease or a continuous spectrum of disease [3]. However, the isolation of specific mechanisms must lead to the change of conceptions and must lead to the assertion "a mechanism - a disease" [4].

In addition, other diseases have other immune mechanisms of the disease, and they are identified and clearly specified [5]. Because it presents as a disease with strictly localized pathogenesis, thyroiditis has been included in the category of „organ-specific" immune diseases [2].

The fact that the thyroid is large (thyromegaly or, inappropriately "goiter") or small (thyromicria) has no relevance to the diagnosis: the disease is the same. Some researchers and authors [6] make the inadequate distinction between *Hashimoto's thyroiditis* (thyroiditis with "goiter", i.e., with thyromegaly) and *chronic lymphocytic thyroiditis* (thyroiditis without goiter). This distinction is not based on the correct understanding of thyroid pathogenesis, due to the phenomena associated with ATPO.

The presence of other antibodies, such as antithyroglobuline (ATG), creates problems of nosological taxonomy. But, as ATGs are oriented towards another antigen and because the immune reaction is different, i.e., it is realized through complement, not by cells [2], by adopting the concept of "a mechanism - a disease", it becomes obvious that thyroiditis with ATG is another kind of thyroiditis. Obviously this is true if we accept the concept that Hashimoto's thyroiditis is that thyroiditis due to ATPO.

Another problem arises when Hashimoto's thyroiditis is said to be "sero-negative" [7] because the diagnosis was morphopathological and in the serum there was no known type of antihyroid antibody present. By adopting the concept of "a thyroid immune mechanism - a thyroid immune disease" it is clear that "sero-negative" thyroiditis is or should be not Hashimoto's thyroiditis. It will become another form of thyroiditis, when the antibodies and antigens involved will be discovered.

INTRODUCTION

Thyroid function has been frequently investigated in thyroid autoimmune diseases including in patient cohorts or in specific communities [8-13]. Most studies focus on the evolution from subclinical hypothyroidism to clinical hypothyroidism. Our study was realized to show whether there is an evolution from euthyroidism to hypothyroidism in patients with Hashimoto's thyroiditis. Furthermore, we have correlatively investigated thyroid function together with the evolution of antithyroid antibodies. To date, such an approach has not been described in the literature. Only two studies investigate the level of ATPO in patients with Hashimoto's thyroiditis: in one it is stated the decrease of the level during the treatment [14], in another one it affirms "fluctuating" evolution [8].

We did not find on *pubmed.gov* a study that takes into account, at the same time, the thyroid function correlative with antibody evolution, especially ATPO, as an essential element of pathogenesis, the direct cause of the disease known as Hashimoto's thyroiditis [15]. As a particularity of the fact that ATPO are considered necessary and sufficient element in the diagnosis of Hashimoto's thyroiditis [4], in our previous research we observed ultrasound characteristics of thyroiditis [16] with normal levels of ATPO. Some patients had high levels of anti-thyroglobulin (ATG) antibodies. We considered these patients non-thyroiditis Hashimoto's, but thyroiditis with hyper-ATG.

The study was retrospective, cohort-specific, and shows the evolution of thyroid function and anti-thyroid antibodies in Hashimoto's thyroiditis, hyperATG thyroiditis (T-ATG) and idiopathic myxedema, correlative with Graves-Basedow disease data.

Nowadays patients with thyroiditis live more. There are many patients with this disease over 65 years, considered as conventional criterion for elderly people. We identify a single study which emphasized the evolution in elderly patients with thyroiditis [8].

Therefore, we stressed on this topic: the evolution of thyroid function corroborated with thyroid autoantibodies in patients over 65 years old with thyroiditis.

MATERIALS AND METHODS

This project/study started more than 20 years ago, when both ultrasound machine

and laboratory tests were available in the same time at one patient, for corroboration data. If there were earlier data available in the same format, we used them.

A. The diagnostic

- The diagnostic of the disease.

Hashimoto's thyroiditis (HT) was considered if the patient had: ATPO antibodies above the conventional cut-off of 34 IU/ml; and ultrasound appearance of hypoechogenic, pseudonodular, nonhomogeneous thyroid [16].

If the ATPO level was normal, but the modification was at the level of the anti-thyroglobulin (ATG) antibodies and the ultrasound aspect was for thyroiditis, then anti-thyroglobulin (T-ATG) thyroiditis was considered. The cut off level for ATG normality was also considered at 34 IU/ml.

If a patient was diagnosed with hypothyroidism but he or she did not have elevated levels of ATPO or ATG, as well as no changes (increases) in TRAB antibodies (which define Graves-Basedow disease), and no other clinical cause known to alter thyroid function (e.g., cervical irradiation for lymphoma), then the diagnosis was considered "idiopathic myxedema".

When a patient presented with increased levels of ATPO concomitant with increased levels of TRAB, regardless of thyroid function, two concomitant diagnoses were considered, namely the association between Hashimoto's thyroiditis and Graves-Basedow's disease, according to the "one mechanism- one disease" theory [4].

For all laboratory analyses, commercial kits were used in approved laboratories from Bucharest in the health public system. If the standard curves used different values for normality, the transformation was performed by the simple 3 rule. ATPO and ATG were analyzed by ECLIA-type electrochemiluminescence. TRAB were determined by binding analysis of some immunoglobulin inhibitors in Brahms technique. The cut-off for TRAB was considered 1 IU/l.

Five patterns were observed regarding the evolution of the thyroid autoantibodies: "undulating", "increasing", "decreasing", "unmodified" and "normalized". It was considered that the ATPO/ATG level did not change if the value was not greater/ lower than 15 IU/ml. We considered ATPO/ATG "normalization" when their level fell below the cut-off limit and thus remained as so at the last observation.

- The diagnostic of the syndrome – functional diagnostic

Normal thyroid function was considered to be when TSH level was between 0.4 and 4 mU/ml, associated with a free thyroxine level (free T4 - FT4) between 10 and 20 pmol/l. When TSH was greater than 4 mU/ml and FT4 was normal, subclinical hypothyroidism was considered. When TSH was lower than 0.4 mU/ml and FT4 was normal, subclinical hyperthyroidism was considered.

B. Patients

We investigated a total of 4.668 patients, 2.034 being diagnosed with Hashimoto's thyroiditis (HT), 19.52% being over 65 years-old. Only 253 have been diagnosed with thyroiditis with only antithyroglobuline autoantibodies (T-ATG). Diagnosis of "idiopathic myxedema" was encountered in 142, 35.21% of patients being over the age of 65 years.

We recorded the patients in time, as they were presented in our clinics/offices. Patients were differentiated according to the diagnosis of disease, corresponding to the level of ATPO, ATG, and according to the diagnosis of the syndrome, corresponding to the level of TSH and FT4. The control patients were specifically registered.

The moment of the last recorded consultation was the moment when the material was sent for publication. All patients were informed according to the Helsinki Declaration 1975 and gave their consent.

C. Statistical analysis

Statistical analysis was performed by the Student t test, the X^2 test, the Fisher test (z test), and the linear correlation test, depending on the context. A "P" value <0.05 was considered to indicate significant differences between the groups under analysis. An Excel 2007 file from a Windows 7 or 10 System was used to perform the calculations.

RESULTS

Using the above criteria, we recorded the following data (Tab. I):

1. Hashimoto's thyroiditis: 2034 patients. From these, 397 (19.52%) were over 65 years old.
2. Thyroiditis with hyper-antithyroglobulinemia (T-ATG): 253 patients. From these, 48 (18.97%) were over 65 years old. No difference in prevalence for patients over 65 years old between HT and T-ATG ($z=0.2$; $p=0.83$).
3. Idiopathic myxedema: 142 patients. From these, 50 (35.21%) were over 65 years old. There is an important difference between this nosological entity and HT/T-ATG. The prevalence of older patients is very high ($z>-4.4$; $p<0.001$).
4. In the Control group we registered 2125 patients, of which 567 (26.68%) were over 65 years old. In this group, there are also older patients that in HT/T-ATG ($z=-5.4$; $p<0.001$).

a) Age

Age at first diagnosis in Hashimoto's thyroiditis is slightly older than the age in T-ATG thyroiditis, but statistically insignificant. In contrast, the first diagnosis in idiopathic myxedema is rather late; age was significantly higher than in other forms of thyroiditis ($p<0.001$). However, in the group of patients with idiopathic myxedema, we also recorded 7 children aged 6-15 years (see standard deviations of the groups). The control patient's age was also a little higher than that of thyroiditis.

That means that the symptomatology in thyroiditis is easier to be recognized by a doctor or by patient herself/himself, and the patient consult earlier an endocrinologist for establishes the problem/the diagnostic.

b) Gender

In classical thyroiditis the ratio Female/ Male = 14.13, with 7.18% men. In the T-ATG, the ratio F/M is slightly lower = 12.31, with 8.12% men (no statistical difference, p=0.5). In the idiopathic myxedema we have the ratio F/M = 4.26, with more men, 23.48%; the statistical significance is z=-8.3, p<0.001. The sex/gender ration in older patients (over 65 years) did not differed comparing with the entire thyroiditis group (7% vs. 6.5%; 8% vs. 6.5%; 23.5% vs. 22%). Even in the control group the ratio is not statistical significant (15% vs. 18%).

c) Autoimmune associations

An important feature of patients with autoimmune diseases is that they associate one or more such diseases. In earlier analyses, we described these associations in Hashimoto's thyroiditis, ATG thyroiditis and idiopathic myxedema, as well as the difference from control patients (for TH, T-ATG and idiopathic myxedema, the test X^2>24, p<0.001) [4]. Thyroid diseases investigated have a 2-fold higher prevalence of immune associations than the presence of immune/autoimmune impairment in control patients.

In HT, the prevalence of immune association for patients over 65 years old are slightly lower than in adult patients (18% vs. 27%, p=0.054, NS).

In idiopathic myxedema the prevalence of immune association in patients over 65 years old were double than in adult patients (44% vs. 22%, p=0.08). The association with another autoimmune disease was observed in 32 cases (22.54%), with 14 patients over 65 years old (43.75%). The prevalence for all idiopathic myxedema was slightly lower than in HT and T-ATG, but without major significance. On the other hand, the prevalence of an immune association is very high in patients over 65 years old.

In the control group, the immune association prevalence in patients over 65 years old is slightly higher than in adult patients (19% vs. 12%, NS).

The prevalence of an immune/autoimmune association in T-ATG (no. 61, 24.11%) is not different from clastic thyroiditis, or idiopathic myxedema. In the patients over 65 years old, this association had a lower prevalence (no=18, 13.11%); p=0.0016, z=3.17.

d) Thyroid volume and nodularization

Hashimoto described in 1912 a nosological thyroid disease with hypothyroidism and thyromegaly. However, in HT there are also thyromicria.

For all patients with classical TH, the volume of the thyroid, measure by ultrasound, was recorded as follows:

- Normal thyroid volume: 1268 patients (62.34%);

- Small thyroid, named also thyromicria: 107 patients (5.26%). All patients with thyroid disease were registered with hypothyroidism! The prevalence of thyromicria in patients over 65 years old was higher: 9% vs. 5%; z=-2.9, p<0.001.
- High thyroid volume, named also thyromegaly: 659 patients (32.4%). The prevalence of thyromegaly in patients over 65 years old was reduced, only 20%; z=4.8, p<0.001.

Therefore, in elderly patients with HT there is the trend to decrease the volume of thyroid.

In patients with T-ATG, the thyroid volume was as follows:

- Normal: 242 patients (95%), a higher prevalence that in HT p<0.001, z=-7.9);
- High (thyromegaly): 5 patients (1.58%), a lower prevalence that in HT (p<0.001, z=5.86);
- Small (thyroid disease): 6 patients (2.37%), a lower prevalence than in classical thyroiditis (p=0.04, z=4.4).

From the point of view of the thyroid volume, there is no difference between elderly patients vs. younger ones with T-ATG.

In all patients with idiopathic myxedema, the thyroid volume was registered, as follows:

- Normal thyroid volume: 126 patients (62.34%);
- Thyromicria: 22 patients (15.49%). Is an important difference from other thyroid entities, especially with HT, z=-7.1, p<0.001. From these, only 3 patients (13.64%) were over 65 years old (difference nonsignificant). These results are hard to interpret.
- Thyromegaly: 0 patients. This phenomenon is very interesting, and dissociates idiopathic myxedema from HT and T-ATG.

Some patients presented a/more thyroid nodule association.

The elderly patients with HT had a higher prevalence of this association than the entire patients with this entity (14.86% vs. 10.57%; z=-2.47, p=0.013).

T-ATG is more associated with a thyroid nodule than HT (27.67% vs. 10.57%; z=-7.7, p<0.001). However, in T-ATG, the prevalence of thyroid nodules in elderly is the same as in all patients with this nosological entity (27.14% vs. 27.67%).

In idiopathic myxedema the number of patients with nodules are lower (9.15%), but the prevalence of nodules among elderly was very high (38.46%; z=-3.15, p=0.0019).

In control group there were many patients with thyroid nodule (41.69%), since this group was made especially from patients with thyroid disorders not registered as thyroiditis. The prevalence of thyroid nodules among elderly patients was high, too (45.15%).

In our patients it seems that nodularization increases with age.

The data related to the structure of thyroid from the control group could not be used to compare with the thyroid entities described above, because the control group was quite inhomogeneous: patients with thyroid nodules, normal, patients with radio-

intervention on the chest and neck. Therefore, a common analysis of these patients was inappropriate.

CONCLUSIONS

After more than 20 years of observation, in cases of Hashimoto's thyroiditis, respectively 5 years, in those with hyper-ATG thyroiditis, no changes in thyroid function are observed. This suggests that most patients with euthyroidism will remain euthyroid all their lives. The older patients have the same pattern. Patients with T-ATG and hyperthyroidism (6.3%) appeared to be associated with Graves-Basedow's disease in much lower prevalence than the phenomenon observed in TH: only 50% had TRAB positive. The older patients with this association reach a prevalence of 8.33%, no statistical difference. Almost all patients with hyperthyroidism became normothyroid under the antithyroid treatment. In 5 years only 5 relapses were registered. In older patients hyperthyroidism was under control, no relapse. About 3% of the hyperthyroid patients became spontaneous hypothyroid.

All these data suggests that an autoimmune association should be a factor to trigger the attention on the thyroid disorder, conducting the patient earlier to the doctor and conducting the doctor to make an earlier diagnosis.

Older patients with Hashimoto's thyroiditis and related conditions demonstrate some specific patterns of evolution if thyroid function that warrant further investigation.

Conflicts of interest

The authors declare no conflicts of interest.

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Tab. I Clinical and biological data from patients with Hashimoto's thyroiditis, thyroiditis with ATG (T-ATG), idiopathic myxedema, and control at diagnostic time

	Classical Hashimoto's thyroiditis (thyroiditis with hyper-ATPO-emia)		Thyroiditis with only hyper-ATG-emia (ATPO normal) (T-ATG)		Idiopathic myxedema (hypothyroidism with normal ATPO and normal ATG		Control group	
	All patients	Patients over 65 years	All patients	Patients over 65 years	All patients	Patients over 65 years	All patients	Patients over 65 years
Number	2034	397 (19.52%)	253	48 (18.97%)	142	50 (35.21%)	2125	567 (26.68%)
Age								
Average	50.29		50.30		55.33		53.23	
Standard Deviation	15.63		15.56		20.62		17.46	
Median	51		51		60 ($p < 0.01$)		55	
ATPO								
Average	675.77	625	9.18		8.43		8.10	
Standard Deviation	1262	1139.5	7.64		6.60		6.98	
ATG								
Average	448.08	641	330.2	341.23	8.25		8.47	
Standard Deviation	1127.5	1539	886.7	768.2	8.16		9.61	
Gen								
Women	1888	373	234	45	115	41	1847	477
Men	146 (7.18%)	24 (6.43%)	19 (8.12%)	3 (6.66%)	27 (23.48%)	9 (21.95)	278 (15.05%)	90 (18.88)
Thyroid function								
Euthyroidism	946 (46.51%)	181 (45.59%)	181 (71.26%)	27 (56.25%)	0	0	1940 (91.29%)	499 (88%)
Hypothyroidism	831 (40.86%)	182 (45.8%)	57 (22.47%)	17 (35.41%)	142	50 (100%)	44 (2.07%)	14 (2.49%)
Hyperthyroidism	257 (12.64%)	34 (8.56%)	16 (6.3%)	4 (8.33%)	0	0	141 (6.64%)	54 (9.5%)
Thyroid nodule (>1 cm) associated	215 (10.57%)	59 (14.86%)	78 (30.83)	19 (27.14%)	13 (9.15%)	5 (38.46%)	886 (41.69%)	256 (45.15%)
Thyroid volume								
Thyromegaly	659 (32.4%)	80 (20.15%)	5 (1.98%)	3 (60%)	0	0		
Thyromicria	107 (5.26%)	36 (9%)	6 (2.37%)	2 (33%)	22 (15.49%)	3 (13.64%)		
Immune/Autoimmune association	555 (27.29%)	104 (18.7%)	61 (24.11%)	8 (13.11%)	32 (22.54%)	14 (43.75%)	259 (12.19%)	49 (18.91%)