Available online at www.sciencedirect.com
ScienceDirect
Metabolism Clinical and Experimental 59 (2010) 896–900
Metabolism
Clinical and Experimental
www.metabolismjournal.com

Prevalence of thyroid dysfunctions in systemic lupus erythematosus

Alessandro Antonelli[a,*], Poupak Fallahi[a], Marta Mosca[b], Silvia Martina Ferrari[a], Ilaria Ruffilli[a], Alessandro Corti[c], Erica Panicucci[d], Rossella Neri[b], Stefano Bombardieri[b]

[a]*Metabolism Unit Department of Internal Medicine, University of Pisa, 56100 Pisa, Italy*
[b]*Rheumatology Unit Department of Internal Medicine, University of Pisa, 56100 Pisa, Italy*
[c]*Department of Experimental Pathology, University of Pisa, School of Medicine, 56100 Pisa, Italy*
[d]*Department of Surgery, University of Pisa, 56100 Pisa, Italy*

Received 3 August 2009; accepted 14 October 2009

Abstract

The association of systemic lupus erythematosus (SLE) and thyroid autoimmunity has been reported by several studies in a wide range of variability. However, from a review of the literature, discrepant results have been reported. The aim of the study was to evaluate the prevalence of clinical and subclinical thyroid disorders in patients with SLE vs sex- and age-matched controls. Thyroid hormones and the presence of antithyroid antibodies were tested and thyroid ultrasonography was performed in 213 patients with SLE vs 426 sex- and age-matched controls, from the same geographic area, with a well-defined status of iodine intake. The odds ratio for subclinical hypothyroidism for female patients with SLE with respect to controls was 4.5 (95% confidence interval [CI], 2.5-8.4); for antithyroid peroxidase antibody (AbTPO) positivity, it was 2.6 (95% CI, 1.7-4.1); and for thyroid autoimmunity, it was 2.9 (95% CI, 2.0-4.4). The mean values of thyroid-stimulating hormone and AbTPO were higher in female SLE patients than in controls ($P < .01$). A significantly ($P < .01$) higher prevalence of clinical hypothyroidism and Graves disease was observed in female SLE patients than in controls. No significant difference between SLE patients and controls was detected with regard to free triiodothyronine and thyroxine. In our series, 3% of SLE patients had "nonthyroidal illness syndrome" vs 0 control. Thyroid function and AbTPOs should be tested and ultrasonography should be performed as part of the clinical profile in SLE patients. Subjects at high risk (women, positive AbTPOs, hypoechoic, and small thyroid) should have thyroid function follow-up and appropriate treatment in due course.

1. Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by chronic inflammation and the production of autoantibodies directed against numerous antigens [1,2].

The association of SLE and thyroid autoimmunity has been reported by several studies in a wide range of variability. However, from a review of the literature, the following considerations arise:

1. Many studies do not have an appropriate control group to evaluate the relative risk of hypothyroidism [3-9].
2. Most studies reported a higher prevalence of thyroid autoimmunity in SLE patients than in controls, but discrepant results have been reported about the prevalence of different antithyroid autoantibodies [10].
3. A high prevalence of hypothyroidism (clinical or subclinical) has been reported by most studies, but in a wide range of variability (from 4% to 21%) [11].
4. Discrepant results have been reported about hyperthyroidism and Graves disease [11].
5. Euthyroid sick syndrome has been reported by some studies [6], but not in others [3,4].
6. Thyroid ultrasonography, which had been progressively becoming one of the most important tools in the diagnosis of thyroid disorders, has been evaluated in SLE patients only in few studies [12].
7. Furthermore, there are no studies taking into account iodine intake, which is a major determinant of thyroid disorders and including a complete thyroid workup.

For other thyroid disorders such as central hypothyroidism, only anectodal reports are present in the literature [13].

* Corresponding author. Tel.: +39 050 992318; fax: +39 050 553414.
E-mail address: a.antonelli@med.unipi.it (A. Antonelli).

0026-0495/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.metabol.2009.10.010

The aim of our study was to evaluate the prevalence of clinical and subclinical thyroid disorders in a wide group of patients with SLE by assessing thyroid morphology at ultrasound examination and detecting thyroid hormones as well as the presence of antithyroid antibodies, in comparison with an age-matched control group from the same geographic area with a well-defined status of iodine intake, which is a major determinant of thyroid function and morphology [14].

2. Materials and methods

2.1. SLE patients

Two hundred thirteen SLE patients consecutively referred to the Rheumatology Unit of the University of Pisa were recruited into the study.

Diagnosis of SLE was made according to the 1997 revised American College of Rheumatology classificative criteria [15]. The duration of SLE was 11 ± 9 years (minimum, 1; maximum, 30; median, 10). Median disease activity by ECLAM (European Consensus Lupus Activity Measurement) was 5. Treatments performed in SLE patients were recorded. Secondary Sjögren syndrome was diagnosed following the criteria proposed by the American-European Consensus Group [16].

2.2. Control group–general population

Each of the SLE patients eligible for the study was matched, by sex and age and in relation to the residence in an iodine-deficient area, 1-to-2 with a control group of subjects of the background population from the same geographic area (northwest Tuscany). This control group was extracted from a larger sample of 1950 subjects in a population-based survey of thyroid disorders [17]. Iodine intake differs within Tuscany, and reliable data on local iodine intake based on urinary iodine excretion are available [14]. Extraction of either control group from the original population was performed by finding the closest age match (±3 years) to each case within either sex. When more than one age match was available per case, the choice was made at random. Subjects with history of rheumatic diseases were excluded from the control group.

All patients and controls underwent a complete clinical evaluation, with special attention to risk factors for thyroid disorders (family history of thyroid disease and residence in iodine-deficient areas). Demographic characteristics of patients with SLE and controls are reported in Table 1. The SLE patients and controls had similar distributions by sex and age by the matching procedure. The majority of SLE patients and control subjects had resided in an iodine-deficient area for 20 years or more, with no significant difference between the 2 groups (Table 1).

Table 1
Demographic characteristics of patients with SLE or controls

	Controls (iodine deficient)	SLE	*P*
n	426	213	
Age (y)	39 ± 14	41 ± 15	NS
Men-women (n)	24/402	12/201	NS
Iodine deficiency (%)	58‡	53*,†	NS
Familial thyroid disease (%)	33‡	27*	NS
Smokers (%)	20	18·	NS

NS indicates not significant.
$P < .05$ by χ^2:
* SLE vs iodine deficient.
† SLE vs iodine sufficient.
‡ Iodine deficient vs iodine sufficient.

2.3. Ultrasonography of the neck

Thyroid ultrasonography was performed both in patients and in controls. Neck ultrasonography was performed by the same operator using an Esaote AU5 (Esaote S.p.A., Florence, Italy) with a sectorial 7.5-MHz transducer. The physician conducting the ultrasound examination was blinded to the results of laboratory tests. Thyroid volume was calculated using the ellipsoid formula, as described [18-20]. The presence of hypoechoic and dyshomogeneous echogenicity was arbitrarily rated at 3 levels (0 = normal echogenicity, 1 = slight hypoechoic and dyshomogeneous pattern, and 2 = severely hypoechoic and dyshomogeneous pattern) to evaluate structural abnormalities of thyroid tissue associated with thyroid autoimmunity [18-20]. Thyroid autoimmunity was diagnosed by ultrasonography in the absence of positive antithyroglobulin (AbTg) or antithyroid peroxidase antibodies (AbTPO).

2.4. Thyroid blood flow

Thyroid blood flow (TBF) by color-flow Doppler (CFD) was studied in all patients [19,20]. The CFD pattern was defined as follows: (*a*) normal (or type 0), when TBF was limited to peripheral thyroid arteries; (*b*) type I, when TBF was mildly increased; (*c*) type II, when TBF was clearly increased; and (*d*) type III, when TBF was markedly increased [19,20].

2.5. Laboratory evaluation

Laboratory evaluation included measurement of serum levels of thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), AbTg and AbTPO titers, and anti–TSH-receptor autoantibodies (TRAb). Circulating FT3 and FT4 were measured by commercial radioimmunoassay kits (AMERLEX-MAB FT3/FT4 Kit; Amersham, Little Chalfont, Buckinghamshire, United Kingdom). Serum TSH (DiaSorin, Stillwater, MN), AbTPO, and AbTg (ICN Pharmaceuticals, Costa Mesa, CA) were evaluated by immunoradiometric assay methods. The TRAb were measured in patients with the use of a radioreceptor assay (Radim; Pomezia, Rome, Italy) (reference range, 0-1 UI/mL).

For AbTg and AbTPO, positivity was set at greater than 100 and greater than 100 UI/mL, respectively. Values are given as mean ± SD for normally distributed variables.

The study was approved by the institutional ethics committee, and all subjects gave their informed written consent to participate.

2.6. Statistical analysis

Because the female sex is a well-recognized risk factor for thyroid disorders, levels of TSH, FT3, FT4, AbTPO, and AbTg were compared only among subjects of the same sex. Mean group values were compared by using 1-way analysis of variance for normally distributed variables; otherwise, the Mann-Whitney *U* test was used. The χ^2 test or the relative risk was used to compare categorical variable.

3. Results

3.1. Results in female SLE and female controls

Serum TSH and AbTPO levels were significantly higher in SLE patients than in the control group (Table 2). *Subclinical hypothyroidism* (defined as TSH >3.6 μU/mL with FT4 and FT3 within reference range) such as *clinical hypothyroidism* (defined as TSH >3.6 μU/mL with FT4 less than the reference range) was significantly more common in SLE patients than in controls. The mean value of TSH was 5.6 ± 4.1 μU/mL (range, 3.7-16.8) in SLE patients with subclinical hypothyroidism, 27.5 ± 37.4 μU/mL (range, 15.3-87) in patients with clinical hypothyroidism, and 4.5 ± 3.1 μU/mL (range, 3.6-10.5) in control subjects with subclinical hypothyroidism. The prevalence of subjects with positive AbTPO autoantibodies was significantly higher in the SLE group than in controls (Table 2). A thyroid hypoechoic pattern, a sign of inflammatory involvement of thyroid tissue [18-20], was more frequent in SLE patients than in controls.

On the whole, indices of thyroid autoimmunity (AbTg, AbTPO, or ultrasonographic diagnosis of thyroiditis) were significantly more frequent in SLE patients than in controls (Table 2). In contrast, there was no statistically significant difference in the prevalence of *subclinical hyperthyroidism* (defined as TSH <0.2 μU/mL with FT4 and FT3 within reference range) among female patients (Table 2). The prevalence of Graves disease [18] (established from the clinical presentation: presence of a diffuse goiter, varying in size from normal to very large; thyroid hormones [*clinical hyperthyroidism* defined as TSH <0.2 μU/mL with FT3 greater than the reference range] and thyroid autoantibodies measurements [presence of TRAb]; and/or thyroid ultrasonography [decreased, dyshomogeneous echogenicity, and diffuse goiter]) was significantly higher in female patients with SLE (Table 2) than in controls. No case of clinical hyperthyroidism was observed among controls. Thyroid volume was lower even if not significantly in SLE patients than in controls, whereas *thyroid enlargement* (defined as a thyroid volume >20 mL) was not significantly different in the 2 groups.

The odds ratio for subclinical hypothyroidism for female patients with SLE with respect to controls was 4.5 (95% confidence interval [CI], 2.5-8.4); for AbTPO positivity, it was 2.6 (95% CI, 1.7-4.1); and for thyroid autoimmunity, it was 2.9 (95% CI, 2.0-4.4).

Table 2
Comparison of thyroid status among female subjects with SLE and controls

	SLE	C	*P*
	F	F	
No. of patients	201	402	
Age (y)	42 ± 15	39 ± 14	NS
TSH (μU/mL)	3.6 ± 4.1	1.5 ± 1.6	.01
FT4 (ng/dL)	9.1 ± 6.2	12.2 ± 3.1	NS
FT3 (pg/mL)	3.1 ± 1.2	3.2 ± 1.4	NS
AbTg (UI/mL)	157 ± 164	38 ± 131	NS
AbTPO (UI/mL)	194 ± 653	65 ± 127	.01
Subclinical hypothyroidism	16.9%	4.2%	<.001
Clinical hypothyroidism	5.9%	0	<.001
Subclinical hyperthyroidism	4.4%	2.9%	NS
Graves disease	3/198 (1.5%)	0	.01
AbTg+	15.4%	11.1%	NS
AbTPO+	27.6%	12.5%	<.001
Hypoechoic pattern	29.8%	13.1%	<.001
Thyroid autoimmunity	34.7%	15.1%	<.001
Thyroid volume (mL)	9 ± 5	12 ± 11	NS
Thyroid volume >20 mL	5.8%	9.7%	NS
Thyroid volume <6 mL	12.0%	3.3%	<.001

Antithyroglobulin antibodies >100 UI/mL = AbTg +; antithyroperoxidase antibodies >100 UI/mL = AbTPO +; thyroid autoimmunity = AbTg+, or AbTPO+, or ultrasonographic diagnosis of thyroiditis. F indicates female subjects; C, controls.

3.2. Results in male SLE patients and male controls

The prevalence of male patients with positive AbTPO and the mean AbTPO titer in SLE group was higher, even if not significantly, than in controls (Table 3). On the whole, indices of thyroid autoimmunity (AbTg, AbTPO, or ultrasonographic diagnosis of thyroiditis) were more frequent in SLE men than in control individuals. One case of subclinical hypothyroidism was observed in SLE patients; no case of clinical hyperthyroidism was found.

3.3. General results

In each group (Tables 2 and 3), any kind of thyroid disorders had a higher prevalence in women than in men, with the exception of *thyroid enlargement* (defined as thyroid volume > 20 mL), which was, as expected, more frequent in men because thyroid volume is physiologically higher in men [18,19]; but no significant difference was shown in their prevalence between SLE and control men (Tables 2 and 3).

When pooling data of female and male SLE patients (Table 4), hypothyroidism was significantly associated with the presence of AbTPO, a low thyroid volume (<6 mL), a hypoechoic pattern, and the presence of thyroid autoimmunity (no relationship was found with the other thyroid parameters).

Table 3
Comparison of thyroid status among male subjects with SLE or controls

	SLE	C	P
	M	M	
No. of patients	12	24	
Age (y)	41 ± 12	43 ± 16	NS
TSH (μU/mL)	2.3 ± 3.2	1.3 ± 0.8	NS
FT4 (ng/dL)	9.6 ± 4.6	11.7 ± 2.4	NS
FT3 (pg/mL)	3.2 ± 0.7	3.5 ± 0.9	NS
AbTg (UI/mL)	56 ± 132	22 ± 97	NS
AbTPO (UI/mL)	123 ± 178	27 ± 61	NS
Thyroid volume (mL)	15 ± 12	18 ± 15	NS
Subclinical hypothyroidism	1/11 (9%)	0%	NS
AbTg+	16.6%	8.3%	NS
AbTPO+	25%	12.5	NS
Hypoechoic pattern	25%	8.3%	NS
Thyroid autoimmunity	25%	12.5%	NS
Thyroid volume >20 mL	8.3%	16.6%	NS
Thyroid volume <6 mL	0	0	NS
Subclinical hyperthyroidism	0	0	NS

Antithyroglobulin antibodies >100 UI/mL = AbTg +; antithyroperoxidase antibodies >100 UI/mL = AbTPO +; thyroid autoimmunity = AbTg+, AbTPO+, or ultrasonographic diagnosis of thyroiditis.

The CFD pattern in SLE patients (0 in 60%, type I in 31%, type II in 8%, and type III in 1% of patients) was similar to that of controls.

Secondary Sjögren syndrome was identified in 13% of SLE patients: there was no statistical difference in the prevalence of thyroid autoimmunity in SLE patients with or without secondary Sjögren syndrome.

"Nonthyroidal illness syndrome," also known as the *low T3 syndrome* or *euthyroid sick syndrome* (defined as low serum FT3, normal to low FT4, high reverse T3, and normal TSH), was observed in 6 (3%) SLE patients and in 0 control ($P < .01$).

No case of central hypothyroidism was observed.

4. Discussion

Clinical studies demonstrated a high prevalence of thyroid autoimmunity in patients with SLE; however, many of these studies do not have an appropriate control [3-8].

Table 4
Relationship between hypothyroidism (TSH >3.6 μU/mL) and other thyroid parameters in patients with SLE

	TSH >3.6 μU/mL	TSH <3.6 μU/mL	P [a]
AbTPO >100 UI/mL	71%	24%	.001
AbTPO <100 UI/mL	29%	76%	
Thyroid volume <6 mL	26%	4%	.001
Thyroid volume >6 mL	74%	96%	
Hypoechoic pattern, yes	81%	11%	.001
Hypoechoic pattern, no	19%	89%	
Thyroid autoimmunity, yes	94%	31%	.001
Thyroid autoimmunity, no	6%	69%	

[a] χ^2.

Furthermore, other parameters such as iodine status and thyroid morphology that are well known to be able to influence thyroid function have not been studied, and the prevalence of hyperthyroidism remains controversial [11].

The results of our study, using more tests and more sensitive methodology, in a larger group of 213 SLE patients matched with 426 controls, with a similar exposition to iodine deficiency, demonstrate a significantly higher prevalence for clinical and subclinical hypothyroidism (with a prevalence of 6% and 17%, respectively) in female SLE patients than in controls. It should be stressed that the control group was a sample of the general population of Central Italy, so the present series is a case-control study and not an epidemiologic survey. However, the prevalence of hypothyroidism in the control women was substantial (4.2%) and fully in the range of the reported age-adjusted prevalence rates for the Italian population [17], indicating that the control group was not biased toward a lower hypothyroidism prevalence in comparison with the general population and that the current results agree closely with those reported by population-based surveys, which showed 8% prevalence for subclinical hypothyroidism in women older than 40 years [21]. Interestingly, mean TSH value was significantly higher in female SLE patients than in controls. The prevalence of clinical hypothyroidism reported in the literature ranged from 3.9% to 21.4% with a median 6.6%, [11] which is a value very similar to that found in our SLE patients (5.9%).

Autoimmune phenomena are often present in patients with SLE. The percentage of antithyroid antibodies ranged from 21% [10] to 47% [12] in different studies.

This wide range may be at least partially explained by application of steroids and immune-suppressive drugs in SLE patients and by the different sex and age composition, and iodine intake of SLE patients. Population studies have shown the prevalence of AbTPO to be around 10% in women (range, 10%-15%); and it increases with age [21], similarly to the observed prevalence in our female controls (Table 5). The prevalence of AbTg from population studies has been reported to be around 10% in women (range, 10%-15%) [17,21], which is similar to that observed in our female controls (Table 5). A higher prevalence of thyroid autoantibodies was observed in our female SLE patients (Table 5).

The presence of antithyroid antibodies was found in more than two thirds of SLE patients with hypothyroidism. Moreover, hypothyroidism in SLE patients is significantly associated with a thyroid hypoechoic pattern and a small thyroid volume. These findings suggest that autoimmunity is very important in the pathogenesis of hypothyroidism and in

Table 5
Prevalence of AbTg and AbTPO in the general population [17,21], in controls, and in patients with SLE

	General population	Controls	SLE
AbTPO	10% (range, 10%-15%)	12.5%	27.6%
AbTg	10% (range, 10%-15%)	11.1%	15.4%

SLE patients, and that ultrasonography is able to detect morphologic alterations of the thyroid tissue that are associated with a higher risk of hypothyroidism.

The exact incidence of hyperthyroidism in patients with SLE is unknown, ranging in different studies from absence to 8.9% [4,22-24].

In our study, a significantly higher prevalence of Graves disease, of clear autoimmune origin, was observed in female SLE patients, whereas no significant difference was observed for subclinical hyperthyroidism, mainly related to nodular goiter with functionally autonomous nodules.

We did not find any case of central hypothyroidism in SLE patients, suggesting that the cases of central hypothyroidism reported in the literature were incidental cases [13].

In our SLE patients, FT4 and FT3 levels were not significantly different from those of controls, even if the mean FT4 level in female SLE patients was slightly lower than in controls, in agreement with a higher prevalence of hypothyroidism in SLE patients.

The prevalence of nonthyroidal illness syndrome, also known as the *low T3 syndrome* or *euthyroid sick syndrome*, among SLE patients is also controversial. In fact, whereas some authors did not report any case of nonthyroidal illness syndrome [23], in others, a prevalence ranging from 5% to 47.8% has been observed [3,4,6,24].

In our series, 3% of SLE patients had nonthyroidal illness syndrome. This could be explained by the relatively high disease activity of patients included in this study; in fact, in critically ill patients, pronounced alterations in the hypothalamic-pituitary-thyroid axis occur without any evidence for thyroid disease. Triiodothyronine decreases and reverse T3 increases within a few hours of the onset of disease. Severity and duration of disease are related to the magnitude of these changes [25].

Thyroid volume in controls is fully in the range of the reported age-adjusted volume for the Italian population living in areas of slight iodine deficiency [17] and is not significantly different from that observed in SLE patients, with similar exposition to iodine deficiency.

The results of our study in a large group of SLE patients demonstrate a significantly higher prevalence of AbTPO, ultrasonographic findings of thyroid autoimmunity, clinical and subclinical hypothyroidism, and Graves disease than in a very large group of controls with a similar iodine status. Thyroid function should be tested and ultrasonography should be performed as a part of the clinical profile in SLE patients. Those at high risk (women, positive AbTPO, hypoechoic, and small thyroid) should have thyroid function follow-up and appropriate treatment in due course.

References

[1] Mosca M, Bombardieri S. Disease-specific quality indicators, guidelines, and outcome measures in systemic lupus erythematosus (SLE). Clin Exp Rheumatol 2007;25(6 Suppl 47):107-13.

[2] Griffiths B, Mosca M, Gordon C. Assessment of patients with systemic lupus erythematosus and the use of lupus disease activity indices. Best Pract Res Clin Rheumatol 2005;19:685-708.

[3] Miller FW, Moore GF, Weintraub BD, et al. Prevalence of thyroid disease and abnormal thyroid function test results in patients with systemic lupus erythematosus. Arthritis Rheum 1987;30:1124-31.

[4] Boey ML, Fong PH, Lee JS, et al. Autoimmune thyroid disorders in SLE in Singapore. Lupus 1993;2:51-4.

[5] Sram K, Fustar V, Prus V, et al. Changes in thyroid function in systemic lupus erythematosus, progressive systemic sclerosis and rheumatoid arthritis. Reumatizam 1994;41:1-4.

[6] Park DJ, Cho CS, Lee SH, et al. Thyroid disorders in Korean patients with systemic lupus erythematosus. Scand J Rheumatol 1995;24:13-7.

[7] Pyne D, Isenberg DA. Autoimmune thyroid disease in systemic lupus erythematosus. Ann Rheum Dis 2002;61:70-2.

[8] Biró E, Szekanecz Z, Czirják L, et al. Association of systemic and thyroid autoimmune diseases. Clin Rheumatol 2006;25:240-5.

[9] Appenzeller S, Pallone AT, Natalin RA, et al. Prevalence of thyroid dysfunction in systemic lupus erythematosus. J Clin Rheumatol 2009; 15:117-9.

[10] Vianna JL, Haga HJ, Asherson RA, et al. A prospective evaluation of antithyroid antibody prevalence in 100 patients with systemic lupus erythematosus. J Rheumatol 1991;18:1193-5.

[11] Blich M, Rozin A, Edoute Y. Systemic lupus erythematosus and thyroid disease. Isr Med Assoc J 2004;6:218-20.

[12] Tsai RT, Chang TC, Wang CR, et al. Thyroid disorders in Chinese patients with systemic lupus erythematosus. Rheumatol Int 1993;13: 9-13.

[13] Hashimoto K, Asaba K, Tamura K, et al. A case of lymphocytic infundibuloneurohypophysitis associated with systemic lupus erythematosus. Endocr J 2002;49:605-10.

[14] Donati L, Antonelli A, Bertoni F, et al. Clinical picture of endemic cretinism in central Appennines (Montefeltro). Thyroid 1992;2: 283-90.

[15] Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1725.

[16] Vitali C, Bombardieri S, Jonsson R, et al. Classification criteria for Sjogren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis 2002;61:554-8.

[17] Antonelli A, Ferri C, Pampana A, et al. Thyroid disorders in chronic hepatitis C. The Am J Med 2004;117:10-3.

[18] Antonelli A, Fallahi P, Nesti C, et al. Anti-CD38 autoimmunity in patients with chronic autoimmune thyroiditis or Graves' disease. Clin Exp Immunol 2001;126:426-31.

[19] Antonelli A, Rotondi M, Fallahi P, et al. Increase of interferon-gamma inducible alpha chemokine CXCL10 but not beta chemokine CCL2 serum levels in chronic autoimmune thyroiditis. Eur J Endocrinol 2005;152:171-7.

[20] Antonelli A, Rotondi M, Fallahi P, et al. High levels of circulating CXC chemokine ligand 10 are associated with chronic autoimmune thyroiditis and hypothyroidism. J Clin Endocrinol Metab 2004;89: 5496-9.

[21] Vanderpump MP, Tunbridge WM. Epidemiology and prevention of clinical and subclinical hypothyroidism. Thyroid 2002;12:839-47.

[22] Goh KL, Wang F. Thyroid disorders in systemic lupus erythematosus. Ann Rheum Dis 1986;45:579-83.

[23] Mader R, Mishail S, Adawi M, et al. Thyroid dysfunction in patients with systemic lupus erythematosus (SLE): relation to disease activity. Clin Rheumatol 2007;26:1891-4.

[24] Viggiano DP, da Silva NA, Montandon AC, et al. Prevalence of thyroid autoimmune disease in patients with systemic lupus erythematosus. Arq Bras Endocrinol Metabol 2008;52:531-6.

[25] Peeters RP. Non thyroidal illness: to treat or not to treat? Ann Endocrinol (Paris) 2007;68:224-308.