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Original article

# Hashimoto thyroiditis may be associated with a subset of patients with systemic sclerosis with pulmonary hypertension

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ABSTRACT

*Introduction:* Recent studies show an association between autoimmune thyroiditis and systemic sclerosis (SSc) and suggest that this condition may interfere with the ES phenotype. However these studies evaluate the autoimmune thyroiditis as a whole and none of them specifically addresses Hashimoto's thyroiditis (HT) in SSc.
*Objective:* To investigate the presence of HT in SSc patients and its possible association with disease manifestations.
*Methods:* Clinical manifestations of hypothyroidism, TSH and anti-thyroid auto antibodies (anti-TPO. anti TBG and TRAb) were studied in 56 patients with SSc. SSc patients with HT were compared with SSc patients without thyroiditis.
*Results:* HT was observed in 19.64% of patients with SSc. No association was observed between HT and the different forms of disease or profile of autoantibodies. Likewise, there was no difference between the mean modified Rodnan score and presence of Raynaud's phenomenon, scars, digital necrosis, myositis, arthritis, sicca symptoms, esophageal dysmotility and scleroderma renal crisis when the groups were compared. On the other hand, patients with HT had higher frequency of pulmonary hypertension in relation to patients without HT (66.6% *vs* 22.5%, p = 0.016).
*Conclusions:* In the studied sample patients with ES and HT had higher prevalence of pulmonary hypertension. Long-term follow-up studies with a larger number of TH and SSc patients are needed to confirm these data.



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## Tireoidite de Hashimoto pode estar associada a um subgrupo de pacientes de esclerose sistêmica com hipertensão pulmonar

*Palavras-chave:*
Esclerose sistêmica
Esclerodermia
Tireoidite de Hashimoto
Hipertensão pulmonar

RESUMO

*Introdução:* Estudos recentes mostram associação entre tireoidites autoimunes e esclerose sistêmica (ES), e sugerem que essa condição pode interferir no fenótipo da ES. Entretanto, esses estudos avaliam as tireoidites autoimunes como um todo e nenhum deles aborda especificamente a tireoidite de Hashimoto (TH) na ES.

*Objetivo:* Investigar a presença de TH em pacientes com ES e sua possível associação com as manifestações da doença.

*Casuística e métodos:* Manifestações clínicas de hipotireoidismo, TSH, T4 livre e anticorpos antitireoidanos (anti-TPO, anti TBG e TRAb) foram pesquisados em 56 pacientes com ES. Pacientes com ES e TH foram comparados com pacientes com ES sem tireoidite.

*Resultados:* TH foi observada em 19,64% dos pacientes com ES. Não foi encontrada associação entre a TH e as diferentes formas de doença ou com o perfil de autoanticorpos. Da mesma forma, não houve diferença entre a média do escore de Rodnan modificado e entre a presença de fenômeno de Raynaud, cicatrizes estelares, necrose digital, miosite, artrite, sintomas *sicca*, dismotilidade esofágica ou crise renal esclerodérmica quando os grupos foram comparados. Por outro lado, pacientes com TH apresentaram maior frequência de hipertensão pulmonar quando comparados a pacientes sem TH (66,6% *vs* 22,5%; p = 0,016).

*Conclusões:* Na amostra de ES estudada, a TH está associada a uma maior prevalência de hipertensão pulmonar. Estudos de seguimento a longo prazo, englobando um número maior de pacientes com ES e TH, são necessários para confirmar esses dados.



## Introduction

The association among autoimmune diseases is common, regardless if they are organ-specific or systemic.[1] Thus, it is necessary that the physician attending these patients be aware of possible associations, not only for an early diagnosis of such entities, but also to understand more completely the clinical manifestations that these patients may have.

Although there is no clear explanation for the association between autoimmune diseases, it is assumed that there is a genetic predisposition to a common immune defect in many of them.[1] Among other possibilities, the exposure to some eventual infectious or environmental agent that acts as a triggering factor of several diseases may be implicated.[1]

Hashimoto's thyroiditis (HT) is the most common autoimmune disease of the thyroid, being considered as a prototype of organ-specific autoimmune diseases.[2] HT presents with varying degrees of glandular dysfunction, presence of antithyroid antibodies and goiter or atrophy of the gland, and a diffuse lymphocytic tissue infiltrate.[2]

On the other hand, SSc is a systemic autoimmune disease characterized by vasculopathy, excessive deposition of collagen in tissues and presence of autoantibodies.[3] The exact role of autoantibodies in SSc is not well defined,[4] but it is known that they can influence the phenotype presented.[4] Indeed, fluctuations in topoisomerase I titles correlate with skin thickening, assessed by the modified Rodnan score, and with disease activity, measured by clinical and laboratory parameters.[5] Interestingly, a subset of patients who developed negativity for this antibody showed less skin thickening, less lung involvement and better survival, when compared to those persistently positive patients.[6]

SSc patients may have antibodies against thyroid antigens, with or without gland dysfunction.[7] A recent meta-analysis showed that thyroid autoimmune disease was the more common organ-specific autoimmunity disease in patients with SSc, with an estimated prevalence of 10.4%.[8] The association of SSc with anti-thyroid peroxidase antibodies is linked to the presence of HLA-DR15.[7] The connection of SSc with other autoimmune diseases also seems to interfere with their phenotype,[4,8] affecting these patients with a milder form of the disease. However, no study has specifically addressed the association of SSc with HT. Thus, the aim of this study was to investigate the presence of HT in SSc patients and its possible association with immunological and clinical profiles of the disease.

## Patients and methods

A cross-sectional study evaluating 56 consecutive patients followed-up at an outpatient clinic of systemic sclerosis in a single tertiary care hospital was conducted. Data were collected from June 2012 to June 2013. All patients recruited met the classification criteria for SSc from ACR/EULAR 2013.[9]

The following manifestations of SSc were addressed: Raynaud's phenomenon, stellar scars, digital necrosis, skin thickening according to the modified Rodnan score,[10] arthritis, myositis, esophageal dysmotility, cardiac involvement, interstitial pneumonitis, pulmonary hypertension and scleroderma renal crisis. Arthritis was considered as present when at least one swollen joint was observed.[11] The diagnosis of