

ARTICLE ORIGINAL/ORIGINAL ARTICLE  
CHRONIC URTICARIA AND AUTOIMMUNE THYROIDITIS

<http://www.lebanesemedicaljournal.org/articles/60-2/original4.pdf>

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Irani C, Jammal M, Asmar G, Hajj H, Halaby G. Chronic urticaria and autoimmune thyroiditis. *J Med Liban* 2012 ; 60 (2) : 88-90.

**ABSTRACT • GOAL :** Idiopathic chronic urticaria may be associated to other auto-immune diseases, in particular thyroiditis. The goal of our study is to show that this association is higher than the incidence of auto-immune thyroiditis in the general population.

**METHODS :** It is a retrospective observational study including 90 patients with chronic urticaria. We calculated the proportion of patients having associated auto-immune thyroiditis based on a level of anti-TPO > 220 mUI/ml.

**RESULTS :** The mean age of patients was 36.7 years with a sex ratio F/H of 2.9/1. The anti-TPO antibodies were positive in 16 patients (17.7%). Eight were euthyroid, seven had hypothyroidism and one had hyperthyroidism with positive anti-TSH receptor antibodies. The percentage of anti-TPO antibodies in the chronic urticaria patients was higher than the control group (17.7 vs 8.7;  $p < 0.01$ ).

**CONCLUSION :** This significant association between chronic urticaria and autoimmune thyroiditis may change the medical practice in Lebanon by including anti-TPO and anti-thyroglobulin antibodies in the workup of patients with chronic urticaria.

#### INTRODUCTION

Urticaria is a common problem affecting up to 25% of the general population. Chronic urticaria is defined by urticarial lesions lasting for more than six weeks; it represents approximately 30% of all types of urticaria [1-2]. Almost 40% of patients with chronic urticaria have associated angioedema [3].

The etiology of chronic urticaria is identified in less than 20% of cases [1-2, 4]. Many studies showed that idiopathic chronic urticaria may be autoimmune [5] with anti-FcεRI antibodies associated in some cases to other autoimmune diseases. In particular autoimmune thyroiditis (presence of anti-microsomal antibodies or anti-peroxidase anti-TPO antibodies) may be found in 3% to 26% of cases with a significant difference compared to the

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Irani C, Jammal M, Asmar G, Hajj H, Halaby G. Urticaire chronique et thyroïdite auto-immune. *J Med Liban* 2012 ; 60 (2) : 88-90.

**RÉSUMÉ • BUT :** L'urticaire chronique idiopathique peut être associée à d'autres maladies auto-immunes, en particulier la thyroïdite. Le but de cette étude est de démontrer une association de la thyroïdite aux maladies auto-immunes supérieure à son incidence dans la population générale.

**MÉTHODES :** C'est une étude rétrospective de type descriptif incluant 90 patients connus avoir une urticaire chronique. Le pourcentage de patients ayant une thyroïdite auto-immune associée a été calculé en se basant sur un taux d'anticorps anti-TPO > 220 mUI/ml.

**RÉSULTATS :** La moyenne d'âge des patients est de 36,7 ans avec un sexe ratio F/H = 2,9/1. Les anticorps anti-TPO étaient positifs chez 16 patients (17,7%). Huit patients étaient euthyroïdiens, sept avaient une hypothyroïdie et un patient était en hyperthyroïdie avec des anticorps anti-récepteurs de la TSH positifs. Le pourcentage des anticorps anti-TPO chez les patients ayant une urticaire chronique était supérieur au groupe contrôle (17,7 vs 8,7;  $p < 0,01$ ).

**CONCLUSION :** Cette association significative entre l'urticaire chronique et la thyroïdite auto-immune pourrait changer la pratique médicale au Liban en incluant les anticorps anti-TPO et anti-thyroglobuline dans les bilans de routine des patients ayant une urticaire chronique.

general population [6-10]. In few studies of refractory chronic urticaria, the treatment with thyroid hormones in euthyroid patients and positive anti-TPO [10], led to a complete remission of the urticaria.

There have been no studies done in Lebanon evaluating the association between chronic urticaria and autoimmune thyroiditis. The goal of our study is to show that this association is higher than the incidence of autoimmune thyroiditis in the general population.

#### MATERIALS AND METHODS

It is a retrospective observational study of patients with chronic urticaria in Lebanon. They were recruited at our allergy/immunology clinic of Hôtel-Dieu de France hospital. We excluded from our study patients with urticarial vasculitis, hereditary angioedema, amiodarone-induced thyroid disease and pregnant women. Ninety patients with chronic urticaria were included. We calculated the propor-

TABLE I MISCELLANEOUS ABNORMAL BLOOD TESTS AMONG THE 90 PATIENTS WITH CHRONIC URTICARIA	
BLOOD TESTS	Number of patients with positive or abnormal result x/y*
ANA	1/10
C3-C4	1/10
Rhumatoid factor	1/2
Hepatitis C	1/2
Abnormal liver function test	1/30
5-HIAA	1/2
<i>Helicobacter pylori</i> serology	1/30
Hypereosinophilia	2/90
AghBs, parasites in stools, cryoglobulinemia, C1-esterase inhibitor	0/10

\* x: number of patients with abnormal result y: number of patients tested

tion of patients having associated autoimmune thyroiditis based on a level of anti-TPO > 220 mUI/ml (Chemiluminescence; Immulite 2000 XPI) [11]. In table I we describe the variant blood work findings in these 90 patients other than anti-TPO.  $\chi^2$  Pearson test or Epsilon test were used for comparing the chronic urticaria patients to the normal population;  $p < 0.05$  confirms a significant difference between the two populations compared.

## RESULTS

Among the 90 patients studied, 67 were women (74.4%) and 23 were men (25.6%) with a sex ratio F/H of 2.9/1. The age of patients varied between 18 and 71 years with a mean of 36.7 years. All patients had urticaria for a variable period between four months and 10 years (mean of 4.2 years  $\pm$  3.8 years). Forty-three patients (47.7%) had associated angioedema and 14 (15.5%) had worsening of their urticaria after taking non-steroidal anti-inflammatory drugs (NSAIDs).

The anti-TPO antibodies were positive in 16 patients (17.7%): 8 of them (50%) were euthyroid, 7 (43.75%) had hypothyroidism and one (6.25%) had hyperthyroidism with

TABLE II RESULTS OF PATIENTS WITH CHRONIC URTICARIA AND THYROID AUTOIMMUNITY	
<b>Patients with positive anti-TPO</b>	<b>16/90 (17.7%)</b>
Euthyroidism	8/16 (50%)
Hypothyroidism	7/16 (43.75%)
Clinical	4/16 (25%)
Infraclinical	3/16 (18.75%)
Hyperthyroidism with positive TSI	1/16 (6.25%)
Patients with positive anti-TG antibodies	7/7 tested
Improvement with thyroid hormone replacement	2/2
<b>TPO:</b> thyroid peroxidase	<b>TSI:</b> thyroid stimulating immunoglobulins
<b>TG:</b> thyroglobulins	

positive anti-TSH receptor (TSI) antibodies (Table II). Two patients were treated with thyroid hormone and had complete remission of urticaria after three months of treatment. Table III describes the general characteristics of patients in reference to the anti-TPO antibodies.

To prove that the 17.7% with positive anti-TPO is a meaningful incidence we compared them to the general population. In a study done by Halaby *et al.* [12] on 684 normal subjects of the Lebanese population, the anti-TPO antibodies were positive in 60 subjects or 8.77%. Comparing the two groups of the Lebanese population by using a  $\chi^2$  test, we found a higher percentage of anti-TPO antibodies in the chronic urticaria patients compared to the control group (17.7 vs 8.7) with a significant difference ( $p < 0.01$ ; Table IV). If we compare our chronic urticaria patients to the normal American population ( $\chi^2$  test) according to NHANES III study [13], we find a higher frequency of autoimmune thyroiditis in our group ( $p < 0.04$ ; Table IV).

## DISCUSSION

Our study is the first of its kind done in Lebanon. Despite the evidence reported in the literature about the association between chronic urticaria and autoimmune thyroiditis, we didn't have evidence of this association in the Lebanese population.

TABLE III GENERAL CHARACTERISTICS OF PATIENTS IN RELATION TO ANTI-THYROID PEROXIDASE			
Variable	All patients (n = 90)	Patients with positive anti-TPO (n = 16)	Patients with negative anti-TPO (n = 74)
Age (years)	18 - 71 36.7 $\pm$ 12.6	19 - 71 39.6 $\pm$ 16	18 - 70 36 $\pm$ 12.3
Sexe ratio F/M	2.9/1	4.3/1*	2.7/1*
Angioedema	43 (47.7%)	12 (75%)**	31 (41.9%)**
Steroid use	25 (27.7%)	8 (50%)***	17 (23%)***
Allergy to aspirin or NSAIDs	14 (15.5%)	1 (6.25%)	13 (17.6%)
Total IgE > 100	36/61 (59%)	4/11 (36.4%)	32/50 (64%)

\* $p < 0.05$  \*\* $p < 0.02$  \*\*\* $p < 0.03$

**TABLE IV**  
COMPARISON OF PATIENTS HAVING ANTI-TPO WITH CU (CHRONIC URTICARIA) AND THE NORMAL POPULATION

	N	%
Present study		
Total number of patients with CU	90	100
Patients with positive anti-TPO	16	17.7
Halaby <i>et al.</i> [12]		
Number of positive anti-TPO observed in the Lebanese population	60*	8.77*
NHANES III [13]		
Number of positive anti-TPO observed in the American population	10**	11**

\* Significant difference with  $p < 0.01$  (comparison between CU patients of our study and the Lebanese population described in the study of Halaby *et al.*).  
\*\* Significant difference with  $p < 0.04$  (comparison between CU patients of our study and the American population as described by NHANES III study).

According to our results, patients with autoimmune thyroiditis have a more severe urticaria, this was previously described in the literature. Can we conclude then that measuring routine TSH and free T4 without measuring antibodies will miss up to 50% of patients who have chronic urticaria with associated autoimmune thyroiditis?

Autoimmunity may play a role in the pathogenesis of chronic urticaria. One of the arguments would be the presence of IgG anti-Fc $\epsilon$ R1 $\alpha$  antibodies on the basophiles of four patients with chronic urticaria in a study done by Hide *et al.* where the direct release of histamine by basophiles and mastocytes played a major role in chronic urticaria [14]. In addition, the remission of chronic urticaria with cyclosporine may be another hint for autoimmune etiology. In a study done by Rumblyrt *et al.*, 7/7 euthyroid patients with autoimmune thyroiditis and chronic urticaria had complete remission of urticaria after four weeks of treatment with thyroid hormones [15]. In our study, two patients who were treated with thyroid hormone had complete remission of urticaria after three months of treatment. The possible mechanism described in this study is that by suppressing the chronic stimulation and inflammation of the thyroid gland resulting in a negative feedback on the TSH, there is a decrease of pro-inflammatory factors release, and decrease of autoantibodies, diminishing the stimulation of mastocytes in response to allergens or physical factors [16].

#### CONCLUSION

We demonstrated the significant association between chronic urticaria and autoimmune thyroiditis in the group studied from the Lebanese population. This study may change the medical practice in Lebanon; anti-TPO antibodies and anti-thyroglobulin antibodies should now be

included in the workup of patients with chronic urticaria. This may even change the management of chronic urticaria in these patients who usually have severe hard to control disease.

Our study, first of its kind in Lebanon, may serve as a backbone to future studies with a higher number of patients with similar presentations.

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