

## Original Research Article

# Association between chronic spontaneous urticaria and thyroid autoimmunity: a case control study from a tertiary care centre

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### ABSTRACT

**Background:** The exact etiology of chronic spontaneous urticaria is unknown in the majority of patients. A subset of chronic spontaneous urticaria can be autoimmune and may be associated with thyroid autoimmunity.

**Methods:** Serum anti thyroid peroxidase (anti-TPO) antibody level and thyroid function tests (TFT) including triiodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) levels were estimated in 100 patients with chronic spontaneous urticaria and 50 controls. Autologous serum skin test (ASST) was done in 84 chronic urticaria patients and 21 patients with high anti-TPO antibody.

**Results:** High anti-TPO antibodies and abnormal thyroid function were seen in 24 (24%) patients each. High anti-TPO antibody levels were seen in nine (18%) and abnormal TFT in 11 (22%) controls. Abnormal TSH was seen in 22 patients (22%) and 6 (12%) controls. Autologous serum skin test was positive in 53 patients with chronic spontaneous urticaria. It was positive in 16 and negative in five out of 21 patients with high anti-TPO antibody levels.

**Conclusions:** Though there was a slight increase in abnormal anti-TPO antibody level and thyroid dysfunction in patients with chronic spontaneous urticaria compared to controls, it was not statistically significant.

**Keywords:** Urticaria, Thyroid autoimmunity, Autologous serum skin test

### INTRODUCTION

Chronic spontaneous urticaria is characterized by itchy, evanescent, erythematous plaques occurring at least twice weekly for more than 6 weeks.<sup>1,2</sup> There are two types of chronic spontaneous urticaria- chronic idiopathic urticaria and chronic autoimmune urticaria. Chronic autoimmune urticaria can be associated with other autoimmune disorders, the most common being thyroid autoimmunity.<sup>3,4</sup> Autologous serum skin test (ASST) is a simple screening test for chronic autoimmune urticaria. ASST has a sensitivity and specificity of 70% and 80% respectively. This study was conducted to determine the association between chronic spontaneous urticaria and thyroid autoimmunity and also to assess the correlation

between the autologous serum skin test and thyroid autoimmunity.

### METHODS

This case control study was conducted in a tertiary care centre from June 2013 to December 2013 to assess the association between chronic spontaneous urticaria and autoimmune thyroid disorders. The study group involved 100 patients with chronic urticaria and 50 controls without urticaria and without thyroid disease. Patients with physical urticaria, urticarial vasculitis, children below 14 years and pregnant and lactating females were excluded from the study. Clearance was obtained from the institutional ethics committee and informed consent

was obtained from each patient. A detailed history was taken including severity of itching, number and duration of wheals, angioedema, precipitating factors and systemic features. Family history of urticaria, thyroid disorders, atopy and autoimmune diseases was also documented.

Complete hemogram, urine and stool examination, blood sugar, liver and renal function tests, serum hepatitis B surface antigen, anti-streptolysin O titre, rheumatoid factor and antinuclear antibody tests were done in all the patients.

Urticaria activity score (UAS) was calculated by adding the pruritus score and wheal score. Pruritus score (severity of pruritus) ranged from zero to three. 0–no pruritus, 1–mild pruritus (present but not annoying or troublesome), 2–moderate pruritus (troublesome but does not interfere with normal daily activity or sleep), 3–severe pruritus (interfere with normal daily activity and sleep). Wheal score (number of wheals) also ranged from zero to three. 0–no wheal, 1–less than 20 wheals in 24 hours, 2–20 to 50 wheals in 24 hours, 3–more than 50 wheals in 24 hours. Total UAS ranged from 0–6.

Autologous serum skin test (ASST) was done in 84 patients who consented to the procedure, three days after stopping antihistamines and three weeks after stopping systemic steroids, using 0.05ml of autologous serum with normal saline as control. It was considered positive after 30 minutes if the serum induced wheal was 1.5 mm larger than the control. Serum triiodothyronine (T3) normal range 0.7-2 ng/ml, thyroxine (T4) normal range 55-135 ng/ml, thyroid stimulating hormone (TSH) normal range 0.2-4 micro IU/ml and anti-thyroid peroxidase antibody (anti-TPO) levels were estimated in 100 patients and 50 controls using enzyme immunoassay. Anti TPO antibody below 30 IU/ml were considered normal.

### **Statistical analysis**

Statistical analysis was performed using SPSS for windows version 18. Mean was compared between the two groups by Mann-Whitney U test. Chi Square test was used for qualitative variables, a p value of <0.05 was considered statistically significant. Odds ratio was also used for comparing the study group and controls.

## **RESULTS**

The age group of chronic urticaria patients ranged from 14-70 years with mean age of 35.3 years and standard deviation (SD) of 12.95. Mean age of control group was 37.9 years with SD of 14.09 and ranged from 15-73 years. The majority of the persons were in the age group of 31 to 40 years in the patients (35%) as well as controls (34%). Out of the 100 patients with chronic urticaria, 75 were women and 25 were men. In the control group, 38 were women and 12 were men.

The duration of urticaria ranged from 2 months to 30 years with the majority having duration of 2 to 3 years (25%). Associated angioedema was present in 63% of the patients. Family history of urticaria was present in 15%, thyroid disease in 15% and atopy in 25%. Five percent of the patients each had a positive rheumatoid factor and presence of antinuclear antibodies in the serum.

Out of the 100 patients, the urticaria activity score was 6 in 55 patients, 5 in 15 patients, 4 in 15 patients, 3 in 10 patients and 2 in 5 patients.

High anti-thyroid peroxidase antibody was seen in 24 (24%) of the chronic urticaria group, and nine (18%) in the control group, but it was not statistically significant. Abnormal thyroid function was observed in 24 (24%) patients and 11 (22%) controls which was also not statistically significant. The characteristics of the study group and the thyroid abnormalities are shown in Tables 1 and 2.

Among the 24 patients with high anti-TPO antibody, 19 (79%) were females and five (21%) were males. The majority of the anti-TPO positive patients were in the age group of 31 to 40 years, and the duration of the disease ranged from 2 months to 15 years. In the anti TPO positive group, 15 had a UAS of 6, two had a UAS of 5, three each had a UAS of 4 and 3 and one patient had a UAS of 1. Angioedema was present in 13 patients (54%) with high anti-TPO antibody and 50 (65.8%) patients with normal anti-TPO antibody. Risk of having angioedema in anti TPO positive chronic urticaria patients compared with anti TPO negative patients (odds ratio) was not significant. Risk of angioedema in chronic urticaria patients with abnormal thyroid function was 2.76 times higher than patients with normal thyroid function. Thyroid dysfunction was seen in only five (20.8%) of the 24 anti-TPO positive patients.

In the chronic urticaria group, ASST was done in 84 patients out of which 53 (63%) were ASST positive and 31 (36.9%) were ASST negative. Angioedema was seen in 32 (60.4%) ASST positive and 20 (64.5%) ASST negative patients.

Among the 24 anti-TPO positive cases, ASST was done in 21 patients of which 16 (76.2%) were ASST positive and 5 (23.8%) were ASST negative. Chronic urticaria patients with high anti TPO antibody had 2.25 times higher chance of having positive ASST compared with control group, but it was not statistically significant.

Of the 21 patients with abnormal TSH, ASST was done in 19 patients, of which 10 patients (52.6%) were ASST positive and nine (47.4%) were ASST negative. Risk of having ASST positivity in chronic urticaria patients with abnormal TSH was 0.59 which was also not significant. Among the 12 patients with elevated TSH, 7 were ASST

positive and five were ASST negative. Among the seven patients with decreased TSH, three were ASST positive and four were ASST negative.

The clinical features and ASST results in the chronic urticaria patients with altered anti TPO antibody and TSH are shown in Tables 3 and 4.

**Table 1: Characteristics of the study group with abnormal thyroid investigations.**

Groups	Mean age (years)	Sex		Number of patients with high anti-TPO antibody	Number of patients with abnormal TFT	Number of patients with abnormal TSH
		M	F			
<b>Patients</b>	35.33	25	75	24	24	21
<b>Controls</b>	37.9	12	38	18	22	12

Anti TPO=anti thyroid peroxidase; TFT=thyroid function test; TSH=thyroid stimulating hormone.

**Table 2: Thyroid function abnormality in the study group.**

Groups	T3		T4		TSH	
	High	Low	High	Low	High	Low
<b>Number of patients</b>	1	1	0	1	13	8
<b>Number of controls</b>	0	0	0	5	6	0

T3=tri iodothyronine; T4=thyroxine; TSH=thyroid stimulating hormone.

**Table 3: Age distribution of patients with thyroid abnormalities and positive autologous serum skin test.**

Age (years)	Patient group (n=100)	Control group (n=50)	High Anti TPO antibody (n=24)	Abnormal TSH (n=21)	ASST Total (n=84)	ASST positive (n=53)
<b>10-20</b>	15	6	2	1	11	6
<b>20-30</b>	23	9	6	6	18	12
<b>30-40</b>	35	14	8	8	31	21
<b>40-50</b>	13	12	5	3	13	10
<b>50-60</b>	9	6	3	2	7	4
<b>60-70</b>	5	2	0	1	4	0
<b>70-80</b>	0	1	0	0	0	0

T3=tri iodothyronine; T4=thyroxine; TSH=thyroid stimulating hormone.

**Table 4: Comparison of urticaria activity score, duration of disease, angioedema and exacerbation with food and drugs among chronic urticaria patients with altered anti TPO antibody, TSH and ASST.**

Groups (number)	UAS 6 (number)	Duration of CU >5years	Angioedema (number of patients)	Exacerbation with food (number of patients)	Exacerbation with drug (number of patients)
<b>High anti TPO antibody (24)</b>	15	7	13	11	7
<b>Normal anti TPO antibody (76)</b>	40	18	50	23	15
<b>Abnormal TSH (21)</b>	11	5	16	7	5
<b>Normal TSH (79)</b>	44	20	47	27	17
<b>ASST Positive (53)</b>	29	16	32	20	11
<b>ASST Negative(31)</b>	14	6	20	11	9

UAS= Urticaria activity score; CU= chronic urticaria; Anti TPO= anti thyroid peroxidase; TSH= thyroid stimulating hormone.

**DISCUSSION**

Unlike most of the previous studies, chronic spontaneous urticaria was not significantly associated with high serum anti TPO antibody or abnormal thyroid function in our study.<sup>5-10</sup> Thyroid function was normal in the majority of patients with high anti-TPO antibody in our study. There was no statistically significant higher prevalence of anti

TPO antibody in the ASST positive patients which also differ from other studies.<sup>11,12</sup>

Thyroid stimulating hormone abnormality was more common in the chronic urticaria group in our study which was consistent with previous studies.<sup>8,13</sup> There was an equal prevalence of thyroid dysfunction among the patients with ASST positivity and negativity which

indicates that thyroid dysfunction was equally common in chronic idiopathic and autoimmune urticaria, unlike previous studies.<sup>14,15</sup>

Chronic spontaneous urticaria was more common in females in our study. Female predilection was more prominent in chronic urticaria with high anti TPO antibody which was consistent with previous studies.<sup>2-7</sup> Severe urticaria was seen in patients with high anti TPO antibody in our study unlike most of the previous studies.<sup>7,16,17</sup> ASST positive patients also had high urticaria activity in our study, in concordance with other reports but unlike other studies where no correlation was found between the severity of urticaria and ASST positivity.<sup>7,10,18-20</sup> There was no difference in the severity of urticaria among patients with normal or abnormal TSH.

Angioedema was more common in patients with thyroid dysfunction but less common in anti-TPO and ASST positive patients in our study unlike other studies where an equal incidence of angioedema in ASST positive and negative patients was found.<sup>10</sup> Exacerbation of chronic urticaria with food and drugs was more in patients with high anti TPO antibody compared to patients with abnormal TSH.

Though most of the studies support the association between chronic urticaria and thyroid autoimmunity, the pathogenic role of antithyroid antibodies in chronic urticaria has not been proven. Treatment of the thyroid abnormality was also not effective in treating most of the patients with chronic urticaria associated with thyroid autoimmunity. So it has been suggested that chronic urticaria and thyroid disease are associated, parallel autoimmune events. Thyroid autoimmunity may develop many years after the onset of chronic urticaria. Therefore periodic follow up and thyroid reassessment is indicated in patients with chronic urticaria.

The limitation of our study was the inability to determine anti-thyroglobulin antibody status owing to financial constraints which could result in missing some of the cases of thyroid autoimmunity.

## CONCLUSION

Chronic spontaneous urticaria is not significantly associated with thyroid autoimmunity and thyroid dysfunction. More severe urticaria is seen in patients with high anti TPO antibody than in patients with thyroid dysfunction. Angioedema is more common in chronic urticaria with thyroid dysfunction than thyroid autoimmunity.

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