# Thyroid autoantibodies in chronic urticaria: A case-control study in a South Indian population

Karjigi Siddalingappa, MD [1]
Sambasiviah Chidambara Murthy, MD [2]
Kallappa Herakal, MD [1]
Madagondanahalli Deepika, MD [1]

1. *Department of Dermatology, Venereology and Leprosy, Navodaya Medical College Hospital and Research Centre, Raichur, Karnataka, India*
2. *Department of Dermatology, Venereology and Leprosy, Vijayanagar Institute of Medical Sciences (VIMS), Bellary, Karnataka, India*

*Corresponding Author:*
*Karjigi Siddalingappa,*
*Professor, Dept. of Dermatology, Venereology and Leprosy.*
*Navodaya Medical College Hospital and Research Centre,*
*Raichur, Karnataka, India*
*E-mail: karjigi267450@yahoo.co.in*

*Received: 22 September 2016*
*Accepted: 26 October 2017*

**Background:** Chronic urticaria (CU) is a common skin disorder that accounts for 15%-20% of dermatological cases. There is growing evidence that some cases of chronic idiopathic urticaria (CIU) are associated with various autoimmune diseases, including thyroid autoimmunity. This study aims to identify the thyroid profile, including thyroid autoantibodies, in patients with CU.

**Methods:** This case-control study included 100 patients with CU and 100 controls without urticaria. Males and females (age range: 20-40 years) who attended the Navodaya Medical College Hospital and Research centre were included. Participants underwent laboratory investigations that consisted of a complete blood count (CBC) thyroid autoantibodies, and other relevant investigations.

**Results:** Patients in the CU group had a male to female ratio of 1:2.1 and a mean age of 31.2 years. The control group had a male to female ratio of 1:1 and a mean age of 35 years. Antimicrosomal antibodies (AMA) were present in 14 (14%) patients, 13 females and 1 male. There were no autoantibodies in any of the control group participants. Among these 14 patients, 5 (35.71%) had elevated serum thyroid stimulating hormone (TSH) and one had coexistent anti-thyroglobulin antibodies. Other associated diseases included diabetes mellitus, human immunodeficiency virus (HIV), and hepatitis B surface antigen (HBsAg) in one patient each.

**Conclusion:** Thyroid autoantibodies may play a role in persistent CU. Screening patients with persistent CU for thyroid functions, including thyroid autoantibodies, may help with proper management.

**Keywords:** urticaria, thyroid, autoimmune, autoantibodies

Iran J Dermatol 2017; 20: 50-53

## INTRODUTION

There is growing evidence of an association between some cases of chronic idiopathic urticaria (CIU) and autoimmune diseases such as thyroid autoimmunity. The association between chronic urticaria (CU) and thyroid disorders is controversial.

Some reports linked CU with hyperthyroidism or hypothyroidism [1]. A recent study found a 30% frequency of thyroid antibodies in patients with CIU, which was higher than earlier studies [2]. Recently, some studies suggested that there might be a link between CU and thyroid autoimmunity [3]. It has been documented that some patients might respond to the administration of thyroid hormones [4]. Therefore, we conducted this study to determine the association between thyroid disorders, especially autoimmune thyroid disorders, and CU.

## MATERIALS AND METHODS

The study subjects consisted of 100 consecutive

 

male and female patients with a clinical diagnosis of CU who attended the outpatient department (OPD). An equal number of age-sex matched patients without urticaria comprised the control group, over a period of 12 months (1st January 2015 to 31st Dec 2015). The Institution's Ethical Committee approved the study and all study participants gave their informed consent.

Exclusion criteria consisted of: associated renal or liver diseases, drug-induced urticaria, pregnant and lactating women, or patients on steroids or other immunosuppressive therapy within 6 weeks before enrollment. A detailed history and clinical examination that included systemic examination was done. Complete hemogram, urine routine, liver function tests, renal function tests, triiodothyronine (T3), thyroxine (T4), thyroid stimulating hormone levels (TSH), thyroid autoantibodies [antimicrosomal antibodies (AMA)], antithyroglobulin antibodies (ATG), serum immunoglobulin (Ig)E levels, antinuclear antibodies, venereal disease research laboratory test (VBRL), hepatitis B surface antigen (HBsAg), hepatitis C, human immunodeficiency virus (HIV), and stool examination were performed for both groups. There were 2 patients who agreed to have an autologous serum skin test (ASST). We used a proforma for data collection and the chi-square test for statistical analysis.

## RESULTS

This study included a total of 100 patients with CU and 100 controls without urticaria. The CU group had a male to female ratio of 1:2.1. Their ages ranged from 20-40 years (mean: 31.2 years). Duration of urticaria ranged from 6 months-4 years. The control group had a male to female ratio of 1:1. Their ages ranged from 20-40 years (mean: 35 years). AMA were present in 14 (14%) patients - 13 females and 1 male. There were no autoantibodies detected in the control group ($P$<0.05). From the 14 patients, 5 (35.71%) had elevated serum TSH levels and one had coexistent ATG. ASST results in the 2 patients were negative. Other associations included diabetes mellitus (1%), HIV (1%), and HBsAg (1%) as summarized in Table 1.

**Table 1.** Summary of findings.

| | Cases (n=100) | Controls (n=100) |
|---|---|---|
| Mean age (years) | 31.2 | 35 |
| M:F ratio | 1:2.1 | 1:1 |
| AMA | 14 | Nil |
| ATG | 1 | Nil |
| Thyroid dysfunction | 5 | Nil |
| Associations | Diabetes mellitus, HIV virus, HBsAg (1 each) | Nil |

AMA: Antimicrosomal antibodies; ATG: Antithyroglobulin antibodies; HIV: Human immunodeficiency virus; HBsAg: Hepatitis B surface antigen

## DISCUSSION

CU is a common skin disorder that affects 0.11% of the general population. It is characterized by recurrent and transitory (<24 hours) pruritic erythematous wheals that present at least twice a week for at least 6 weeks [5]. CIU is the most common type of CU, which comprises up to 90% of all cases. Over 50% of CIU cases are thought to be caused by an autoimmune mechanism [6]. This is supported by the observation that 60% of patients with CIU elicit a wheal and flare response to intradermal autologous serum injections in the ASST [7]. Approximately 50% of patients with CIU have IgG antibodies that are specific for the high-affinity IgE receptor (FceRI) [6,7]. These autoantibodies activate mast cells in the skin, circulating basophils, and the complement system [6]. The factor that causes basophil degranulation is unknown. Hashimoto's thyroiditis may likely be a marker of autoimmunity rather than a direct cause for CU [8].

As early as 1983, Leznoff *et al.* [1] have suggested an association between thyroid autoimmunity and CIU. Although the association of CU and thyroid autoimmunity is not well understood, patients with a positive ASST are more likely to have an association with HLA DR4, autoimmune thyroid disease, prolonged disease course, and possibly less responsive to H1-antihistamine treatment than those with negative ASST [6]. In our series, both patients who consented to the ASST had negative results.

Autoimmune thyroid diseases are the most common organ-specific autoimmune disorders that usually result in dysfunction (hyperfunction, hypofunction, or both) of the thyroid gland [9]. The role of thyroid autoantibodies in physiological changes of CU is highly debatable [10]. Although the pathophysiology of the association is not well understood, it seems that antithyroid antibodies may not be directly responsible for the lesions

seen in CU patients; however, they are probably an indicator of autoimmunity [11]. This autoimmune subgroup of CU patients is frequently referred to as chronic autoimmune urticaria (CAU). CAU patients have autoantibodies directed at the FceR1a receptor located on mast cells and basophils or less commonly against IgE [12]. In the current study, 14% of patients had autoantibodies although a few had thyroid dysfunction in the form of hypothyroidism. Possibly, autoantibodies appear earlier and patients would need to be followed regularly.

Our study showed a female predilection with more than twice the number of females, which was consistent with previous studies [5,13,14]. In an early study by Leznoff *et al.* [1], 12% of patients with urticaria had elevated titers of thyroid antibodies, among whom 88.2% were females. In a later, larger scale study, Leznoff and Sussman [15] reported the results of a survey of 624 CIU and angioedema patients, among whom 90 (12.1%) had high titers of thyroid microsomal antibodies and 44 presented with other clinical and laboratory findings suggestive of autoimmune thyroiditis. Palma-Carlos *et al.* [16] performed a case-control study to evaluate thyroid antibodies in CIU patients. They detected ATG positivity in 22.2% and AMA positivity in 26.8%. However, 93% of the CIU patients had normal thyroid functions. The authors concluded that thyroid antibody and function must be evaluated in all cases of CU. Aamir *et al.* [17] reported elevated titers of ATG and AMA in patients with CU. Our findings of a higher prevalence of thyroid antibodies among patients concurred with these studies. In contrast, Sabroe and Greaves [14] found that thyroid autoimmunity prevalence in CIU patients was not greater than the general population. The difference could probably be due to the small sample size and sampling methods.

The current study results indicated a higher prevalence of AMA than ATG in CU cases compared with controls. This was consistent with the results reported by Aamir *et al.* [17] who demonstrated that AMA had higher prevalence than ATG in his study group. Trbojevic and Djurica [9] and Kandeel *et al.* [8] also reported that the incidence of thyroid dysfunction had a statistical significance in CAU patients. However, thyroid autoimmunity might appear several years after the onset of CU, which would emphasize the importance of follow-up and periodic blood tests for T4/TSH and antithyroid antibodies in CU patients [18]. In contrast, a few studies have found no link between urticarial severity and positivity of autoantibodies [19-22].

Our study was not without limitations. The sample size was smaller and the ASST could not be performed on the majority of patients. Further large, population-based studies may help in understanding the role of thyroid autoantibodies in CU pathogenesis. In conclusion, thyroid autoantibodies may play a role in persistent CU. Screening such patients for thyroid functions, including autoantibodies, may help with suitable patient management.

**Acknowledgement**

We would like to express our appreciation to Sri Ananth, MSc, statistician, for his valuable help with statistical analysis.

## REFERENCES

1. Leznoff A, Josse RG, Denburg J, Dolovich J. Association of chronic urticaria and angioedema with thyroid autoimmunity. Arch Dermatol. 1983; 119 (8):636-640.
2. Najib U, Bajwa ZH, Ostro MG, Sheikh J. A retrospective review of clinical presentation, thyroid autoimmunity, laboratory characteristics, and therapies used in patients with chronic idiopathic urticaria. Ann Allergy Asthma Immunol. 2009; 103 (6):496-501.
3. Dayan CM, Daniels GH. Chronic autoimmune thyroiditis diseases. N Engl J Med. 1996;335(2):99-107.
4. Heymann WR. Chronic urticaria and angioedema associated with thyroid autoimmunity: review and therapeutic implications. J Am Acad Dermatol 1999; 40 (2 Pt 1):229-232.
5. Abd El-Azim M, Abd El-Azim S. Chronic autoimmune urticaria: frequency and association with immunological markers. J Investig Allergol Clin Immunol 2011; 21(7):546-550.
6. Kaplan AP. Chronic urticaria: pathogenesis and treatment. J Allergy Clin Immunol 2004; 114(3):465-474.
7. Hide M, Francis DM, Grattan CE, Hakimi J, Kochan JP, Greaves MW. Autoantibodies against the high-affinity IgE receptor as a cause of histamine release in chronic urticaria. N Engl J Med 1993; 328 (22):1599-1604.
8. Kandeel AA, Zeid M, Helm T, Lillie MA, Donahue E, Ambrus JL Jr. Evaluation of chronic urticaria in patients with Hashimoto thyroiditis. J Clin Immunol 2001; 21(5):335-347.
9. Trbojevic B, Djurica S. Diagnosis of autoimmune thyroid disease. Srp Arh Celok Lek. 2005;133 Suppl 1:25-33.
10. Bansal AS, Hayman GR. Graves disease associated

with chronic idiopathic urticaria: 2 case reports. J Investig Allergol Clin Immunol 2009; 19(1):54-56.

11. Rumbyrt JS, Katz JL, Schocket AL. Resolution of chronic urticaria in patients with thyroid autoimmunity. J Allergy Clin Immunol 1995; 96 (6 Pt 1): 901-905.
12. Vikramkumar AG, Kuruvila S, Ganguly S. Autologous serum skin test as an indicator of chronic autoimmune urticaria in a tertiary care hospital in South India. Indian Dermatol Online J 2014; 5(6):87-91.
13. Caproni M, Volpi W, Giomi B,Fabbri P. Chronic idiopathic and chronic autoimmune urticaria: clinical and immunopathological features of 68 subjects. Acta Derm Venereol. 2004; 84(4):288-290.
14. Sabroe RA, Greaves MD. The pathogenesis of chronic idiopathic urticaria. Arch Dermatol. 1997; 133(8):1003-1008.
15. Leznoff A, Sussman GL. Syndrome of idiopathic chronic urticaria and angioedema with thyroid autoimmunity: a study of 90 patients. J Allergy Clin Immunol.1989; 84(1):66-71
16. Palma-Carlos AG, Palma-Carlos MI. Chronic urticaria and thyroid autoimmunity. Eur Ann Allergy Clin Immunol. 2005; 37(4):143-146.
17. Aamir IS, Tauheed S, Majid F,Atif A. Frequency of autoimmune thyroid disease in chronic urticaria. J Coll Physicians Surg Pak 2010; 20(3):158-161.
18. Zauli D, Deleonardi G, Foderaro S, Grassi A, Bortolotti R, Ballardini G, *et al.* Thyroid autoimmunity in chronic urticaria. Allergy Asthma Proc 2001; 22:93-95.
19. Nettis E, Dambra P, D′Oronzio L, Cavallo E, Loria MP, Fanelli M, *et al.* Reactivity to autologous serum skin test and clinical features in chronic idiopathic urticaria. Clin Exp Dermatol 2002; 27(1):29-31.
20. Kulthanan K, Jiamton S, Gorvanich T, Pinkaew S. Autologous serum skin test in chronic idiopathic urticaria: prevalence, correlation and clinical implications. Asian Pac J Allergy Immunol 2006; 24(4):201-206.
21. Al-Hamamy HR, Hameed AF, Abdulhadi AS. Autologous serum skin test as a diagnostic aid in chronic idiopathic urticaria. ISRN Dermatol 2013; 2013:291524.
22. Nuzzo V, Tauchmanova L, Colasanti P, Alfonso Zuccoli, Annamaria Colao. Idiopathic chronic urticaria and thyroid autoimmunity: experience of a single center. Dermatoendocrinol 2011; 3(4):255-258.