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Original Research Article

A Clinico-Epidemiological Study of Chronic Urticaria and its Association with Thyroid Profile

Anila Sara Thampi[1], Vinma Shetty[2], Abhineetha Hosthahota[3], Anitta Sara Thampi[4]

[1]Assistant Professor, Department of Dermatology, the Oxford Medical College and Hospital, Bangalore, Karnataka, India

[2]Professor, Department of Dermatology, AJ Institute of Medical Sciences, Mangalore, Karnataka, India

[3]Professor, Department of Dermatology, the Oxford Medical College and Hospital, Bangalore, Karnataka, India

[4]Consultant Dermatologist and HOD, Bahrain Specialist Hospital, Bahrain

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Corresponding Author: Dr. Anila Sara Thampi

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Abstract

Background: Urticaria is a disease characterized by noticeable itchy bumps and dark red raised spots or rashes. Several studies have testified to a substantial relation between autoimmune thyroid disease and CU. It was also reported that chronic urticaria patients show a deranged thyroid profile.

Aim and Objectives: The present study aimed to evaluate the pattern of chronic urticaria in patients coming to the OPD and to study the association between chronic urticaria and various thyroid parameters (T3, T4, TSH).

Materials and Methods: This was a hospital-based observational study conducted for a period of 2 years on 144 patients with chronic urticaria between the age groups of 18 and 15 years. The data was collected based on a pre-tested, semi-structured questionnaire. A complete history, clinical examination, and thyroid profile were collected. Data analysis is done using SPSS version 17.0.1. A chi square test was used to test association between chronic urticaria and thyroid profile and selected sociodemographic variables.

Results: In the present study, urticaria was more common in males than females, and their association showed significant ($p = 0.003$). The level of HB and TLC was shown to be highly significant. Atopy was the most common association with urticaria, and their association was shown very high significance ($p<0.0001$). And, chronic urticaria in patients with angioedema was less than in patients with no angioedema, and their association showed very high significance ($p<0.0001$).

Conclusion: This study concludes that male prevalence of the disease is associated with a significant association between the thyroid function test and the prevalence of CU.

Keywords: Chronic Urticaria, Dermographism, Angioedema.

Introduction

Urticaria is a disease characterized by noticeable itchy bumps and dark red raised spots or rashes. The disease is known to affect 15-20% of individuals. Chronic urticaria occurs when the episodes are recurrent for at least 6 weeks, with two episodes per week. [1] Males are less affected by the disease in comparison to females. [2] The research in this field has improved our understanding of autoantibodies, the pathogenesis of the disease, and the background possibility of autoimmune disease.

The autoimmune background for urticaria was suggested in 1983. There was an observation of the relationship between chronic urticaria and thyroid disease. The functional anti-IgE antibodies were detected and thought to function as urticarial wheals. [3] Approximately 30-50% of individuals with chronic urticaria exhibit antibodies against IgE. Chronic urticaria is linked to many forms of autoimmune disease. [4] The majority of chronic urticaria cases are idiopathic. Autoimmunity has been accepted as a contributing factor for the pathogenesis of the disease. [5] There is a possibility that urticaria is triggered by drugs such as opioids, aspirin, anti-inflammatory drugs, alcohol, and ACE inhibitors. 6.7-67% of individuals with chronic urticaria may be exacerbated by aspirin. [4] In the majority of chronic urticaria forms, the mast cells are thought to play the role of effector cells directly or indirectly through other cell types. The development of angioedema and wheals is linked to the release of histamine from the mast cell degranulation. The change in capillary and venule permeability at the local site contributes to

urticaria. The cutaneous mast cell activation derives these changes as they encompass a number of mediators, including histamines. [6] The itching, blistering, and redness are the main characteristics of urticarial plaque. This is sometimes accompanied by a burning sensation. The individual can develop lesions anywhere, and it takes usually 2-3 hours for recovering. The recovery can, in some cases, take 1 day. Skin swelling can suddenly occur in lip and eyelid mucosae in angioedema. The burning and pain are usually at the forefront. The spontaneous regression occurs in 72 hours. [7] The occurrence of edema and erythema in dermographism takes 10-20 minutes post-mechanical trauma. In such a case, if the individual experiences an itchy feeling, the case is considered to be dermatographic urticaria. Nearly 4% of the population is observed to have this condition.

The main characteristic feature of autoimmune disease is the inapt immune response activation against own tissues and cells. There can be involvement at the systemic level, or a specific organ can be the target. [8] In 1907, it was the first time that a link between urticaria and autoimmune disease was highlighted. [9] There have been decades of research to identify the relationship with thyroid disease. The presence of antibodies such as IgG or IgE and antithyroid antibodies TGAbs and TPOAbs are also associated with chronic urticarial. [8]

It is rather easy to diagnose based on clinical appearance and anamnesis. Though, it is also sometimes confused with drug eruptions, viral rashes, connective tissue diseases, photosensitive diseases, urticaria pigmentosa, urticarial vasculitis, and a number of syndromic diseases. It is imperative to obtain detailed anamnesis from the urticaria patient to reach the etiology.

Aims and Objectives: The present study aims to study the pattern of chronic urticaria in patients coming to the OPD and to study the association between chronic urticaria and various thyroid parameters (T3, T4, TSH).

Materials and Methods

This was a hospital-based observational study conducted for a period of two years from November 2018 to November 2019 in the Dermatology OPD in A J Institute of Medical Sciences; Mangalore was enrolled in the study. One hundred and forty-four patients with chronic urticaria in the age group of 18–50 years of both genders were included in the study. The patients were explained regarding the objectives as well as the method of study with informed consent. A pre-tested, semi-structured questionnaire was used for the collection of data along with a complete history, clinical examination, and thyroid profile. Simple random sampling (lottery method) was adopted to select the study subject.

Inclusion Criteria and Exclusion Criteria: Patients who gave consent, both male and female, with chronic urticaria between the ages of 18 and 50, were included in the study. Patients below age 18, above 50 and who refused to give consent, patients on chemotherapy, and patients with acute urticaria were excluded from the study.

Statistical Analysis: Data processing and statistical analysis were done using SPSS 17.0.1 (Statistical Package, Software for Windows, Chicago: SPSS.Inc). A chi square test was used to test association between chronic urticaria and thyroid profile and selected sociodemographic variables.

Results

In this present study, a total of 144 patients were included. Among these included patients, 56.3% were male and 43.6% were female. Maximum of the patients (38.20%) were in the age range of 31 to 40 years, with a mean age of the patients with chronic urticaria in this study being 37.89±7.96 years. The maximum duration of urticaria was below one year (79.20%), followed by 2 years to 5 years (16.7%). In the present study, the maximum age group of patients with dermographism was more than 30 years of age [13 (72.22%)], and their association was shown not to be significant ($p = 0.207$). The study shows that 12.50% of patients' ages had less than 20 years, 25.00% of patients' ages were between 21 and 30 years, 38.20% of patients' ages were between 31 and 40 years, and 24.30% of patients' ages had more than 40 years (table 1). In the present study, 56.30% of male patients and 43.60% of female patients. The maximum duration of CU was below one year (79.20%), followed by 2 years to 5 years (16.7%) (Table 2). The maximum age group of patients with CU was more than 30 years of age [13 (72.22%)], and their association was not significant ($p = 0.207$). In the present study, the maximum duration of urticaria among those who had urticaria was below one year [13 (72.22%)], and their association was shown not to be significant ($p = 0.384$). CU was higher in males [16 (88.9%)] than females [2 (11.1%)], and their association was shown to be significant ($p = 0.003$). In the present study, patients with increased T3 level (table 3) [8 (44.4%)] were less than those with normal T3 level [10 (55.60%)] and normal HB level [6 (33.3%)]. Their association was not significant ($p = 0.515$). In the present study, 100.0% of CU patients had normal (Table 3) T4 level [18 (100.0%)], and their association was shown not to be significant ($p = 0.093$). CU patients with increased TSH levels [1 (5.60%)] were less than the normal TSH levels [17 (94.40%)] and normal HB levels [6 (33.3%)]. Their association was not significant ($p = 0.896$).

Patients with decreased HB were more [8 (44.4%)] than the increased HB level [4 (22.20%)] and nor-

mal HB level [6 (33.3%)]. Their association was shown to be very highly significant (p<0.0001). In the present study, patients with increased TLC levels [5 (27.8%)] were less than those with normal TLC levels [13 (72.20%)], and their association was shown to have high significance (p<0.0001). Patients with chronic urticaria with normal eosinophils (Table 5) [2 (11.1%)] were less than the patients with increased eosinophils [16 (88.9%)], and their association was shown to be very significant (p<0.0001). In the present study, atopic patients with dermographism positivity (Table 6) were higher [12 (66.7%)] than patients with no atopy [6 (33.30%)], and their association was shown to have high significance (p<0.0001). In the present study, patients with angioedema [4 (22.2%)] were less than the patients with no angioedema [14 (77.80%)], and their association was significantly very high (p<0.0001) (Table 7). The mean ± SD age of urticaria patients was more [37.89±7.96] than the mean±SD age of non-urticaria patients [34.03±9.89], and the mean difference of age was shown not to be significant (p = 0.116).The mean duration of urticaria was more [1.71±1.85] than the non-urticaria [1.35±1.79], and the mean difference of age was shown not to be significant (p = 0.437).

Table 1: Showing Age Distribution in the Present Study

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	<= 20 Years	18	12.5	12.5	12.5
	21-30 Years	36	25.0	25.0	37.5
	31-40 Years	55	38.2	38.2	75.7
	> 40 Years	35	24.3	24.3	100.0
	Total	144	100.0	100.0	

Table 2: Duration of Urticaria

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	3 Months – 6 Months	55	38.2	38.2	38.2
	6 Months - 1 Year	59	41.0	41.0	79.2
	1 Year - 2 Years	3	2.1	2.1	81.3
	2 Years - 5 Years	24	16.7	16.7	97.9
	> 5 Years	3	2.1	2.1	100.0
	Total	144	100.0	100.0	

Table 3: Association between CU and T3 and T4 Levels

			Dermographism		Total
			No	Yes	
T3	Increased	Count	46	8	54
		% Within T3	85.2%	14.8%	100.0%
		% Within Dermographism	36.5%	44.4%	37.5%
	N	Count	80	10	90
		% Within T3	88.9%	11.1%	100.0%
		% Within Dermographism	63.5%	55.6%	62.5%
Total		Count	126	18	144
		% Within T3	87.5%	12.5%	100.0%
		% Within Dermographism	100.0%	100.0%	100.0%

Table 3a

			Dermographism		Total
			No	Yes	
T4	Decreased	Count	18	0	18
		% Within T4	100.0%	0.0%	100.0%
		% Within Dermographism	14.3%	0.0%	12.5%
	Increased	Count	9	0	9
		% Within T4	100.0%	0.0%	100.0%
		% Within Dermographism	7.1%	0.0%	6.3%
	N	Count	99	18	117
		% Within T4	84.6%	15.4%	100.0%
		% Within Dermographism	78.6%	100.0%	81.3%
Total		Count	126	18	144
		% Within T4	87.5%	12.5%	100.0%
		% Within Dermographism	100.0%	100.0%	100.0%

Table 3b

Table 4: CU with TSH Levels

			Dermographism		Total
			No	Yes	
TSH	Increased	Count	8	1	9
		% With TSH	88.9%	11.1%	100.0%
		% Within Dermographism	6.3%	5.6%	6.3%
	N	Count	118	17	135
		% With TSH	87.4%	12.6%	100.0%
		% With Dermographism	93.7%	94.4%	93.8%
Total		Count	126	18	144
		% With TSH	87.5%	12.5%	100.0%
		% With Dermographism	100.0%	100.0%	100.0%

Table 5: CU with Eosinophil Count

			Dermographism		Total
			No	Yes	
Eosinophils	Eosinophils increased	Count	20	16	36
		% Within Eosinophils	55.6%	44.4%	100.0%
		% Within Dermographism	15.9%	88.9%	25.0%
	N	Count	106	2	108
		% Within Eosinophils	98.1%	1.9%	100.0%
		% Within Dermographism	84.1%	11.1%	75.0%
Total		Count	126	18	144
		% Within Eosinophils	87.5%	12.5%	100.0%
		% Within Dermographism	100.0%	100.0%	100.0%

Table 6: CU with Atopy

			Dermographism		Total
			No	Yes	
ATOPY	No	Count	119	6	125
		% With ATOPY	95.2%	4.8%	100.0%
		% With Dermographism	94.4%	33.3%	86.8%
	Yes	Count	7	12	19
		% With ATOPY	36.8%	63.2%	100.0%
		% With Dermographism	5.6%	66.7%	13.2%
Total		Count	126	18	144
		% With ATOPY	87.5%	12.5%	100.0%
		% With Dermographism	100.0%	100.0%	100.0%

Table 7: Patients with Angioedema and Dermographism Findings

			Dermographism		Total
			No	Yes	
Angioedema	No	Count	126	14	140
		% within Angioedema	90.0%	10.0%	100.0%
		% within Dermographism	100.0%	77.8%	97.2%
	Yes	Count	0	4	4
		% within Angioedema	0.0%	100.0%	100.0%
		% within Dermographism	0.0%	22.2%	2.8%
Total		Count	126	18	144
		% within Angioedema	87.5%	12.5%	100.0%
		% within Dermographism	100.0%	100.0%	100.0%

Discussion

Urticaria ('hives' or 'nettle rash') is defined as the sudden appearance of erythematous, itchy, wheals of various sizes, with or without angioedema, that disappears without any trace in less than 24 hours. Urticaria affects the superficial skin layers (papillary skin dermis), whereas angioedema involves the subcutaneous, deeper reticular dermis, and subcutaneous tissue. Urticaria and angioedema can occur at the same time or can occur separately. The occurrence of the symptoms for more than 6 weeks is chronic urticarial. [10] In this present study, a total

of 144 patients were included. Among these included patients, 56.3% were male and 43.6% were female. However, this difference was found to be non-significant. This finding was contrasting with the finding from previous studies. Most studies conducted in the past reported a female prevalence among chronic urticaria patients.

Gattey et al. (2015) reported that in patients with chronic spontaneous urticaria, the presence of autoimmune diseases is common. This study reported a higher number of female patients with a female: male ratio of 4:1. [11] The present study reported a maximum number of patients who belonged to the younger age group. In a previous study, it was reported that the peak age of patients with CU (Chronic Urticaria) reported in this same study was between 40 years and 49 years. After the stratification of age in the study every two decades, it was reported that 35.4% of the subjects had a peak age of 40 years to 59 years. 26.8% of the patients were in the age group of 20 years to 39 years. The male to female ratio was reversed in the age group of 50 years and more. Most of the female patients with CU were in the age group of 20 years and 49 years. [12]

In a study conducted in India among 500 patients suffering from urticaria, it was reported that almost 83% of the patients had physical stimuli associated with the condition. 37% of the patients were found to be suffering from physical urticaria. The majority of the patients had symptomatic dermographism, followed by cholinergic urticaria and cold urticaria. This study pointed out that performing a physical stress test is important in these patients for proper identification of the urticaria condition. [13] A study by *Myriyath et al. (2021)* reported the duration of chronic urticaria between 2 years and 3 years. Half of the patients (53%) showed the presence of dermographism. The most common etiological factor was food (34%), followed by hose dust exposure (28%). Among other etiological factors, sweat, pressure, drugs, sunlight, heat, and stress were also shown to be aggravating factors. 63% of the patients reported the presence of angioedema. The duration of urticaria as reported in this study ranged from 2 months to 30 years. This study reported atopy and thyroid disorder as the most common co-morbid conditions. [14]

In contrast to the present study finding, *Gattey et al. (2015)* reported an average duration of 8.8 years with a mean age of onset of disease of 36 years.[11] No significant association between the free T3 and T4 levels was reported in this study. The TSH level was increased more in the healthy controls than in the CU patients. In contrast to the present study finding *Okba et al. (2015)*, TSH levels were found to be higher in ASST-positive patients when compared with the healthy controls. Similarly, free T3 level was shown to be lower in ASST patients than in ASST-negative and healthy controls. [15]

Confino-Cohen et al. (2012) studied a total of 12,778 patients who had visited the physician's chamber for allergic reasons. The data on the diagnosis of patients were collected, and similarly, control data from another study population was also collected. This study reported that in patients with CU, the prevalence of hyperthyroidism, hypothyroidism, and autoimmune thyroid diseases was higher. The patients with CU had a higher mean platelet count, an increased number of antinuclear antibodies, and also were recognized positive rheumatoid factor. This study thus reported a strong correlation between the CU and the autoimmune diseases. The presence of autoimmune diseases indicates a positive association between the pathogenesis of both diseases. [16] *Asero et al. (2003*) reported that in CU patients it is not abnormal to detect normal thyroid functions. In this study, 257 CU patients were included; among them, 26% had the presence of circulating anti-thyroid antibodies. Interestingly, in 46 patients, no such difference in the thyroid hormone levels was detected. Moreover, 16 patients had a reduced thyroid function test with a lower free T4 level and an increased thyroid-stimulating hormone level. This study also reported a prevalence ranging from 12% to 27% in the study population.[17]

Conclusion

Chronic urticarial occurs more frequently in adults, in the third to fifth decade of their lives. It was reported in previous studies that chronic urticaria is associated with several autoimmune diseases. In the present study, the clinic epidemiological profile of chronic urticaria was reported, and also its association with thyroid diseases was investigated. This study reported a male prevalence of the disease. This study also reported a significant association between the thyroid function test and the prevalence of CU. The most common manifestation as reported in this study is dermographism. Moreover, a statistically significant association between the CU and the TLC was also observed in the present study. The most common association with CU was atopy. The patients with angioedema were shown to be less in the population with CU. In conclusion, we believe that the production of autoantibodies is indicative of a heightened immunologic response that may influence the development and/or persistence of CU. Moreover, we agree with the recommendations of previous authors that thyroid testing, including measurement of antithyroid antibodies, should be routinely considered in patients with CU refractory to standard therapy and that treatment with thyroid suppression be considered in patients with severe urticaria and evidence of TA despite a euthyroid state.

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