

# Clinico - etiological study of chronic Urticaria and the role of autologous serum skin test in the diagnosis of chronic idiopathic Urticaria

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## ABSTRACT

**Introduction:** Urticaria is a common pruritic skin disorder that affects 15 to 25% of individuals at some point of their life time. It is one of the most frustrating problem to the affected victim because it produces severe physical and emotional distress. Likewise, it poses a serious therapeutic dilemma to the attending dermatologist because of its chronicity and refractory nature of lesions to the treatment.

**Materials and Methods:** A total number of one hundred patients of either sex with history suggestive of chronic urticaria reporting to the out patient clinic of Dermatology, Venereology and Leprology (DVL) department during the period of two years from April 2009 to March 2011, constituted the subjects for the present study.

**Results:** The patients were in the age group of 11-65 years with maximum number (33%) being in the 21-30 years age group. Females (66%) outnumbered the males (34%) in the series. Majority of the patients (53%) belonged to the urban area and were literate (91%). Duration of the disease varied from 6 weeks to 5 years and the most commonly observed was from 1-2 years. 58% of the patients had only Urticaria and the remaining 42% had Urticaria and angioedema.

**Conclusion:** From the present study, it is concluded that the etiology is not clear in large number of patients and hence labelled as chronic idiopathic urticaria. Autologous serum skin test (ASST) constitutes one of the important screening test for autoimmune urticaria.

**Keywords :** Urticaria, Angioedema, Autoantibodies, Autologous serum skin test.

## INTRODUCTION

The Urticarias are characterized by short-lived swellings (wheals) on the skin due to leakage of plasma from capillary dilatations. A hive or wheal is an erythematous or pale, nonpitting edematous plaque that changes in size and shape by peripheral extension or regression during few hours or days

that the individual lesion exits. The evolution of urticaria is a dynamic process. New lesions evolve as old ones resolve. Hives result from localized capillary vasodilation, followed by transudation of protein-rich fluid into the surrounding tissue; they resolve when the fluid is slowly reabsorbed. Hives may be surrounded by a clear or red halo. Thicker plaques that result from massive transudation of fluid into the dermis and subcutaneous tissue are referred to as angioedema.

Angioedema presents as pale or pink swellings, mainly on the face, around the eyelids and lips usually but other areas of the body may also be affected. Mucosal swellings occur inside the oral cavity on the buccal mucosa, tongue, pharynx and larynx. The lesions may be preceded by itching or tingling sensation although they are not always pruritic. Urticaria and angioedema may be associated at times with headache, dizziness, nausea, vomiting, abdominal pain, diarrhea and arthralgia. Both these conditions may coexist although angioedema may occur in some patients without urticarial lesions due to the deficiency of enzyme C1 esterase inhibitor in hereditary or acquired form.

Urticaria is traditionally classified into acute and chronic based on the duration. When urticaria is present daily or almost daily for less than 6 weeks, it is termed as 'acute urticaria'. If urticaria occurring every day or twice per week, lasting longer than 6 weeks, it is termed as 'chronic urticaria'<sup>1,2</sup>. The cause of acute urticaria is possible to determine in many cases. However, in chronic urticaria it is clear in only 5% to 20% of cases and as such these patients constitutes a major problem in the diagnosis and treatment.

Based on clinical features and trigger factors many variants of urticaria have been described such as, ordinary urticaria, physical and cholinergic urticarias, urticarial vasculitis, contact urticaria, angioedema without wheals, idiopathic urticaria and other syndromes resembling urticaria or angioedema.

**MATERIALS AND METHODS :** The present study was conducted on a total number of one hundred patients of either

sex with history suggestive of chronic urticaria for a period of two years, from April 2009 to March 2011. A provisional diagnosis of chronic urticaria was made after obtaining a detailed history and thorough clinical examination in all the patients. Patient presenting to the OPD with lesions of urticaria of > 6 weeks duration and patients willing to undergo investigations required in the study including autologous serum skin test (ASST) were included and patients with age less than 10 years and patient receiving systemic antihistamines (preceding 7 days) and systemic steroids or other immunosuppressive medications (preceding 2 months) were excluded in our study.

A detailed history of each patient was recorded in the proforma specially designed for the study including the particulars about present complaints and duration of wheals, frequency and time of attacks, seasonal variation, relation with ingestion of food or drugs, relation with physical activity, history of sore throat, fever, cough, joint pains, etc. The presence or the absence of a personal or family history of atopy (asthma, hay fever or atopic eczema), drug history, allergy history and past medical history were also noted.

Complete physical and systemic examination has been carried out in each patient and the relevant clinical characteristics of the disease such as morphology of the lesion, sites of involvement, duration, recurrence and associated angioedema and features of anaphylaxis were noted. Routine haematological investigations including haemogram, absolute eosinophil count were done. Examination of stool and urine were carried out. Special investigations such as liver function tests, renal function tests, VDRL, throat swab culture, antinuclear antibodies, thyroid profile were carried out.

All patients were thoroughly interviewed to record the circumstances, events and precipitating factors attributed by them for the urticarial attack. Food items, exercise, emotional upsets related to the urticarial attacks were noted. Patients were subjected to appropriate tests to confirm the diagnosis of physical urticarias. The diagnosis of chronic idiopathic urticaria was considered in patients when there was no evident cause of urticaria even after conducting detailed history and necessary investigations. Subsequently, all these patients were subjected to ASST after obtaining informed consent. Finally, the results of ASST were correlated with the findings noted in the history and clinical examination of the patient and an interpretation of the relevance of a positive or negative ASST was carried out. Later, they were advised accordingly the treatment for their urticaria.

## RESULTS

In the present study duration of the disease varied from 6 weeks to 5 years and the most commonly (28%) observed was from 1-2 years. Fifty eight percent of patients (58%) had only urticaria and remaining (42%) patients had urticaria and angioedema.

History of atopy was found in 21% patients. Etiological factors were elicited in 46% patients and remaining 54% were idiopathic. Physical urticaria (30.4%) constituted the major etiological factor followed by infections (32.6%), food (21.7%), drugs (11%) and inhalants (4.3%). Among various triggering infective agents, bacterial infections (46.6%) were common. Among physical urticaria patients, dermographism (42.8%) was the most common followed by the remaining constituted contact urticaria (21.4%), cholinergic (14.2%), pressure (14.2%) and solar urticaria (7.1%).

Autoimmune urticaria was observed in 27.7% of chronic idiopathic urticaria patients as indicated by positive ASST results and 60% were females and 40% were males. The age of the patients ranged from 11 to 65 years with maximum number of cases (33%) falling in the 21-30 years age group [Table 1]. A female preponderance is noted with a female to male ratio of 2:1

**Table 1: Distribution of chronic urticaria patients according to the age and sex**

Age Group (years)	Male		Female		Total	
	No. pts	%	No. pts	%	No. pts	%
Up to 10 yrs	-	-	-	-	-	-
11-20 yrs	3	8.8	6	9.1	9	9
21-30 yrs	11	32.3	22	33.3	33	33
31-40 yrs	8	23.5	20	30.3	28	28
41-50 yrs	7	20.5	10	15.15	17	17
51-60 yrs	2	5.8	6	9.1	8	8
61-70 yrs	3	2.9	2	6.06	5	5
Total	34		66		100	100

The duration of the disease varied from > 6 weeks to > 5 years and the most commonly observed duration was between 1-2 yrs [Table 2]. In the present study, 21 patients were found to be atopic of which 13 (61.9%) were males and 8 (38%) were females [Table 3]. Out of total 100 chronic urticaria cases studied, the etiological factors were elicited in only 46 (46%) of individuals and the remaining were idiopathic (54%). Physical urticarias (30.4%) constituted the major group, followed by infections (32.6%) food (21.7%), drugs (11%) and inhalants (4.3%) [Table 4]. ASST was evaluated in 54 chronic idiopathic urticaria patients and the test was positive in 6 males and 9 females with overall positivity of 15 (27.7%) [Table 5].

**Table 2: Distribution of chronic urticaria cases according to duration of disease**

Duration	Male		Female		Total	
	No. pts	%	No. pts	%	No. pts	%
6-12 Weeks	3	8.8	9	13.6	12	12
3-6 Months	4	11.7	11	16.6	15	15
6-12 Months	5	14.7	18	27.2	23	23
1-2 Yrs	13	38.2	15	22.7	28	28
2-4 Yrs	6	17.6	8	12.2	14	14
5 Yrs	3	8.8	5	7.5	8	8
Total	34		66		100	

**Table 3: Distribution of chronic urticaria cases associated with atopy**

Atopy	Male		Female		Total	
	No. pts	%	No. pts	%	No. pts	%
Present	13	38.23	8	12.12	21	21
Absent	21	61.76	58	87.87	79	79

**Table 4: Distribution of chronic urticaria cases according to the etiological factors (n=46)**

Etiology	Male		Female		Total	
	No. pts	%	No. pts	%	No. pts	%
Drugs	2	4.3	3	6.5	5	10.8
Food	6	13	4	8.7	10	21.7
Infections	7	15.2	8	17.3	15	15
Inhalants	1	2.6	1	2.6	2	4.3
Physical	8	17.3	6	13	14	30.4

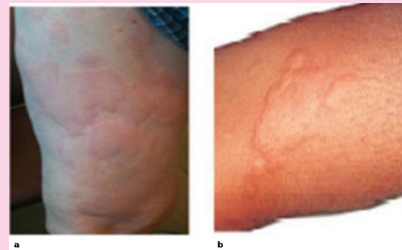
**Table 5: Distribution of chronic idiopathic urticaria cases according to the results of ASST(n=54)**

Asst.	Male		Female		Total	
	No. pts	%	No. pts	%	No. pts	%
Positive	6	33.3	9	25	15	27.7
Negative	12	66.7	27	75	39	72.3
Total	18	100	36	100	54	100

Several studies have been conducted to find out the incidence of autoimmune urticaria which is a subset of chronic idiopathic urticaria (CIU) and they revealed varying results. Asero et al<sup>3</sup> observed an occurrence of auto antibodies in 67% patients whereas Kulthanan et al<sup>4</sup> found an evidence of autoimmune urticaria in only 24.5% of Chronic urticaria (CU) cases. Various Indian studies revealed varying results. Godse<sup>5</sup> and George M et al<sup>6</sup> reported a positive ASST in 26.6% and 34% CU cases respectively. The present series showed positive ASST results in 27.7% of CU cases which is in agreement with the study by Godse. This variation in the results of ASST may be due to sample size taken or because of parameter variation or may be procedure variation.

**Figure1**

**Figure 1:** Clinical photograph showing dermographism. Note appearance of linear wheals surrounded by a flare on firm stroking.

**Figure2**

**Figure 2:** Clinical photographs showing urticaria.

**Figure3**

**Figure 3:** Clinical photograph showing positive reaction with ASST in a patient of autoimmune urticaria, A- Saline, B- Histamine, C-TestSerum.

## DISCUSSION

Urticaria is a common pruritic skin disorder that manifests with varied clinical presentations. In some patients no specific trigger or cause can be identified and as such they are labelled as CIU. Urticaria can occur in any age group, however, chronic urticaria is seen more commonly in adults, whereas acute urticaria is more common in children and young adults. Majority of the chronic urticaria patients studied in the present series are of 21-40 years age group. It compares well with the observation noted by Krupashankar et al<sup>7</sup> and Kulthanan et al<sup>4</sup>. Preponderance of the disease in adults is probably due to their active life styles involving more frequent exposure to environmental triggers.

It is generally believed that patients with atopic diathesis are more prone to develop chronic urticaria (CU). This aspect has been focused in several earlier studies on CU. Positive family history of atopy was found in patients studied by Sarojini et al<sup>11</sup> (26%), Sanjay et al (19%), present series (18%). Dermographic urticaria (physical urticaria) is the most commonly observed factor responsible for CU. It reflects the triple response consisting of a local erythema due to capillary vasodilation, followed by edema and a surrounding flare due to axon reflex induced by dilatation of arterioles. This feature was noted by Champion et al<sup>8</sup> in 8.5% of cases and Humphrey<sup>9</sup> in 9.5% of patients. In contrast to these findings, it was observed in large number of patients (42.8%) in the present series. Perhaps this disparity may reflect variation in the sample size analyzed in different studies.

The association of chronic urticaria with thyroid disorders, provide an indirect evidence of autoimmune origin in CU. Systemic lupus erythematosus (SLE), juvenile rheumatoid arthritis, insulin-dependent diabetes mellitus and celiac disease are other autoimmune disorders reported in association with CU.

Kikuchi et al<sup>10</sup> observed antithyroid antibodies in 27.7% of CU patients; Toubi et al noted thyroid disorder in 12% of CU cases. In the present series, this feature was observed in 31.25% of cases, which is in broad agreement with Kikuchi et al. Variations found in the association of thyroid autoimmunity in different studies may be due to the geographical and ethnic variations in the subjects studied.

Functional histamine-releasing anti Fc $\gamma$ RI autoantibodies and less commonly, anti IgE-autoantibodies have been reported in 30-50% cases of CIU. Patients with autoimmune antibodies have no distinctive diagnostic clinical features and hence the clinical diagnosis depends

on autologous serum skin test. Positive ASST test gives a rough indication of basophil and mast cell histamine releasing propensity of a patient with CIU. It is suggestive but not diagnostic of an autoimmune basis. Positive ASST was observed in 27.7% of CIU cases in the present study which is in broad agreement with the earlier studies investigating autoimmune urticaria (AIU) and ASST (Table 6).

**Table 6: Evaluation of chronic idiopathic urticaria and ASST in different studies**

Author	Year of Study	Positive Asst.
Sabroe et al	1999	33.3%
Asero et al	2001	67%
Nettis et al	2002	41.2%
Caproni et al	2004	34%
Kulthanan et al	2006	24.5%
Godse	2004	26.6%
George M et al	2008	34%
Present study	2010	27.7%

Several conducted studies to find out the incidence of autoimmune urticaria which is a subset of CIU and they revealed varying results [Table 6].

To conclude in a prospective clinico-etiological study of one hundred chronic urticaria patients, the etiology is not clear in large number of patients and hence labeled as chronic idiopathic urticaria. In rest of them the most common etiological agents observed are physical factors, infections, food and drugs etc. in the order of priority. Autologous serum skin test (ASST) constitutes one of the important screening test for autoimmune urticaria.

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