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Original Research Article

Chronic urticaria: a clinico-etiological study and autologous serum skin test role in chronic idiopathic urticaria

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ABSTRACT

Background: Appearance of wheals daily for more than six weeks is chronic urticarial (CU). No cause is identified in about 50-70% of chronic urticaria patients and are labelled as chronic idiopathic urticaria (CIU). The aim of the present study is to study the clinical and etiological pattern of chronic urticaria and to find out the incidence of autoimmune urticaria by performing autologous serum skin test (ASST) in patients with CIU.
Methods: This was a cross sectional study enrolling 100 chronic urticaria patients satisfying including and excluding criteria. The study was done for a period of 1 year. ASST was done in all the CIU patients after recording detailed history, complete physical and systemic examination.
Results: Most of the patients (33%) were in 21-30 years age group with female preponderance (66%). Students (38%) followed by house wives (27%) were majorly involved. 21% patients had history of atopy and 8% had abnormal thyroid function tests. Causative factors noticed in 46% patients and remaining were idiopathic (54%). Infections (32.6%) constituted the major etiological factor followed by physical urticaria (30.4%), food (23.9%), medication (11%) and inhalants (2.1%). In infective agents, 46.6% were bacterial followed by helminthic (33.3%). In 29.6% of CIU patients, the ASST was positive indicating auto-immune urticaria.
Conclusions: The etiology cannot be identified in most number of patients and hence they were labelled as CIU and the common causative agents observed were infections followed by physical urticaria, food and medication. ASST is considered as the relevant screening test to detect autoimmune urticaria.

Keywords: Chronic idiopathic urticaria, Autologous serum skin test, Autoimmune urticaria

INTRODUCTION

Urticaria (nettle rash or hives) is a common disorder that affects the population with life time prevalence of up to 22% and point prevalence of 1%.[1] Urticaria clinically manifest as recurrent, pruritic, pink to red edematous wheals or plaques having pale centre. The urticaria is clinically classified as acute (if duration less than 6 weeks) or chronic (if duration greater than 6 weeks).[2] Urticaria can occur in all age groups, however, in adults chronic urticaria is more common, whereas in children and adolescents acute urticaria is more common.[3] It is more prevalent in middle age group females.[4]

Despite adequate efforts, the cause is evident only in 5% to 10% of chronic urticaria patients. In the classification of urticaria based on etiology, the idiopathic form is more frequent, which constitute up to 70% of the cases.[5] About 30–50% of the chronic idiopathic urticaria (CIU) patients have circulating autoantibodies (released by histamine) to high affinity IgE receptor Fc€R1 present on the mast cells and basophils or less commonly antibodies to IgE. The term autoimmune urticaria (AIU) is used for this subset of

patients.[6] Autologous serum skin test (ASST) is one of the important in-vivo screening test for detection of autoimmune urticaria and this fact has been substantiated in several western studies.[7] ASST has 80% specificity and 70% sensitivity.

The study was conducted to know the clinical and etiological pattern of chronic urticaria and to find out the incidence of AIU by performing ASST in patients labelled as chronic idiopathic urticaria.

METHODS

The present study was done in the dermatology department, ESIC Medical College and Hospital, Hyderabad from January 2019 to December 2019. 100 patients of chronic urticaria of varying age group, who presented to the department, were enrolled for the study.

Inclusion criteria

All the patients with chronic urticaria attending outpatient department (OPD) and who gave consent to undergo investigations whenever necessary including ASST were included in the study.

Exclusion criteria

Patients with age <10 years, pregnant and lactating mothers. Patients receiving oral antihistamines (for preceding week), oral corticosteroids and other immune-suppressive drugs (for last 2 months) were excluded from the study.

A detailed history of each patient including the chief complaints, duration of wheals, frequency of attacks, variation with season, relation with ingestion of food or medication, physical activity were recorded. The history of infections i.e., fevers, sore throat, joint pains, and cough was noted in the proforma. The atopic history (asthma, atopic eczema, hay fever), allergic history and past medication history were also recorded.

In each patient, general physical and cutaneous examination has been done and the following clinical characteristics (morphology, sites of involvement) of disease were noted. Blood investigations like complete blood picture, liver function test, renal function test, thyroid function test were done.

Appropriate tests are done in patients to diagnose physical urticaria. To demonstrate demographic urticaria, scratching of the skin was done by a blunt object; and for cholinergic urticaria cases jogging exercise or running in place for 15 minutes (to increase the core body temperature) was done which provoke urticaria lesions.

When food items are suspected to be the cause of chronic urticaria, the patients were subjected to the diet elimination test which was carried out on an outpatient basis by asking the patient to prepare diet charts to pick up the suspected items of food and then instructed to abstain from that particular food item for two weeks and observe the results. Drug challenge test with low dose of the offending drug was done when the chronic urticaria was suspected due to drugs. Phototesting was done in cases of solar urticaria cases. Urticaria induced by pressure was confirmed by applying pressure on the skin and the patient was instructed to notice the swelling after 4 to 6 hours. All the patients without any etiology were considered as CIU patients and are subjected to ASST after obtaining informed consent.

ASST procedure

2 ml of blood is withdrawn from antecubital vein and allowed to clot at room temperature. It is subjected to centrifugation (2000 rpm for 15 minutes) to separate the serum. Of this serum 0.05 ml is given as intradermal injection into the anterior aspect of forearm. 0.05 ml of normal saline (negative control) is given as intradermal injection 3 to 5 cm apart on the anterior aspect of same forearm. After 30 minutes, wheal and flare response is measured and the one with a diameter of ≥1.5 mm compared to the weal induced by saline is considered as positive ASST.

The collected data was entered into Microsoft excel 2007 software and further analysed using statistical package for the social sciences (SPSS) 20. For descriptive analysis, the categorical variables were analysed by using percentages.

RESULTS

100 patients fulfilling inclusion and exclusion criteria were enrolled in the study. The clinical, epidemiological and etiologic profile in chronic urticaria patients have been evaluated in the present study.

The patients age ranged from 11 to 70 years with most of the cases (33) present in 21-30 years age followed by 31-40 years (28) age. Females were predominant with female to male ratio of 1.9:1 (Table 1). Majority of the chronic urticaria patients (53%) hailed from urban area as shown in Table 2. Majority of chronic urticaria patients (91%) are literate with secondary school level (42%) being the largest educational group (Table 3). Among all the patients, students (39%) were majorly involved, followed by house wives (22%), agricultural laborers (18%), industrial workers (7%) and others (14%) (Table 4). The duration of chronic urticaria disease ranged from 6 weeks to beyond 5 years. 1–2 years duration of urticaria was most common (Table 5).

Chronic urticaria patients with angioedema were seen in 42% and without angioedema in 58% (Table 6).

Atopic history was present in 21% of patients, of them 15 were male and 6 were female patients. 8% patients had abnormal thyroid function test, of them 3 were male and 5

were females (Table 7). In 46 patients out of 100 etiological factors were elicited and remaining 54 patients was considered as CIU patients. In 46 patients infection (32.6%), constituted the major etiological factor, followed by physical urticarias (30.4%), food (23.9%), medication (11%) and inhalants (2.1%) (Table 8).

Among physical urticarias (n=14), dermographism (42.8%) was seen as the most frequent physical urticaria, followed by contact urticaria (21.4%). Cholinergic and pressure urticaria was seen in 14.2% and solar urticaria was seen in 7.1% (Table 9). Among different infections associated with chronic urticaria patients, bacterial (46.6%) were the most common followed by helminthic (33.3%), fungal (13.3%) and viral (6.6%) (Table 10).

ASST was done in 54 CIU patients and found to be positive in 16 patients (29.6%). Among them 7 were males and 9 were females (Table 11).

Table 1: Chronic urticaria patients' distribution based on age and sex.

Age (in years)	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
11-20	2	5.8	7	10.6	9	9
21-30	12	35.3	21	31.8	33	33
31-40	9	26.5	19	28.8	28	28
41-50	8	23.5	9	13.6	17	17
51-60	1	2.9	7	10.6	8	8
61-70	2	5.8	3	4.53	5	5
Total	34		66		100	100

Table 2: Chronic urticaria patients' distribution in rural and urban areas.

Area	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
Rural	15	44.1	32	48.4	47	47
Urban	19	55.8	34	51.5	53	53

Table 3: Chronic urticaria patients' distribution based on educational status.

Educational status	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
Illiterate	4	11.72	5	7.55	9	9
Primary	6	17.58	12	18.1	18	18
Secondary	13	38.10	29	43.8	42	42
Graduate and above	11	32.23	20	30.2	31	31

Table 4: Chronic urticaria patients' distribution based on occupation.

Occupation	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
House wives	-	-	22	33.33	22	22
Students	13	38.2	26	39.3	39	39
Agricultural labourers	9	24.5	9	13.6	18	18
Industrial workers	7	20.5	-	-	7	7
Miscellaneous	5	14.7	9	13.6	14	14

Table 5: Chronic urticaria patients' distribution based on disease duration.

Duration	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
6–12 weeks	4	11.7	8	12.1	12	12
3–6 months	3	8.8	12	18.1	15	15
6–12 months	3	8.8	20	30.2	23	23
1–2 years	15	43.95	13	19.6	28	28
2–4 years	6	17.6	8	12.1	14	14

Continued.

Duration	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
>5 years	3	8.8	5	7.6	8	8
Total	34		66		100	100

Table 6: Chronic urticaria patients' distribution with and without angioedema.

Type	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
Without angioedema	19	55.67	39	58.89	58	58
With angioedema	15	43.95	27	40.77	42	42

Table 7: Chronic urticaria patients associated with atopy and abnormal thyroid function test (TFT).

Atopy	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
Atopy	15	44.1	6	9.06	21	21
Abnormal TFT	3	8.8	5	12.1	8	8

Table 8: Chronic urticarial patients distribution based on etiology (n=46).

Etiology	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
Medication	2	4.3	3	6.5	5	10.8
Food	6	1.3	5	10.8	11	23.9
Infections	7	15.2	8	17.3	15	32.6
Inhalants	1	2.1	0	0	1	2.1
Physical	8	17.3	6	13	14	30.4

Table 9: Physical urticaria patients distribution based on triggering factors.

Type	Male patients	Female patients	Total patients
	Number	Number	Number
Dermographism	2	4	6
Cholinergic	2	-	2
Pressure	1	1	2
Contact	2	1	3
Solar	1	-	1

Table 10: Distribution of chronic urticaria cases associated with various infections (n=15).

Infections	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
Bacterial	3	42.8	4	50	7	46.6
Viral	-	-	1	12.5	1	6.6
Fungal	1	14.2	1	12.5	2	13.3
Helminthic	3	42.8	2	25	5	33.3

Table 11: Distribution of CIU cases based on ASST results (n=54).

ASST	Male patients		Female patients		Total patients	
	Number	%	Number	%	Number	%
Positive	7	38.3	9	25	16	29.6
Negative	11	61.1	27	75	38	70.3

DISCUSSION

Urticaria is a vascular reaction of skin characterised by the appearance of evanescent wheals, angioedema or both. This is a disabling condition and prevents the patient from performing daily activities, with sleep deviation and has psychiatric co-morbidity.[1]

CIU is defined as short lived (<24 hours) pruritic wheals occurring daily for a minimum duration of 6 weeks, without any evident cause.[8]

In the present study, 61% of patients are of 21–40 years age which is in concordance with studies done by Krupashankar et al and Kulthanan et al.[9,10] Predominance of chronic urticaria in this age is may be due to frequent exposure of triggers in their life styles. Chronic urticaria occurs in both sexes, however, female preponderance has been noted in the earlier studies, including the present study with female to male ratio of 1.9:1.

It is generally believed that chronic urticaria is more prone to develop in patients with history of atopy. In the present study, atopic family history was observed in 21% of patients which is similar to studies done by Sarojini et al (26%) and Sanjay et al (19%).[11,12] Abnormal thyroid function tests were observed in 8% of the chronic urticaria patients which is similar to study done by Mamatha et al where 11% is observed.[13]

The disease duration ranged from 6 weeks to 5 years and above, with highest number of cases seen in 1-2 years in the present study. This is in contradiction with the study done by Kulthanan et al who observed the disease duration to vary from 3 months to 9 years.

The incidence of CIU varied in different studies, Humphrey and Sanjay et al noted CIU in 56% cases where as Kulthanan et al noted in 75% cases.[14] Our data showed 54% CIU cases which is in concordance with Humphrey et al and Sanjay et al.

The etiological factors responsible for chronic urticaria have been evaluated in different studies. These include physical stimuli, infections, food, drugs, and autoimmune disorders. In the present study infections (32.6%) were the major etiological factor followed by physical urticarias (30%) and food (22.9%). This is similar to Krupashankar et al who reported an infective focus in 38% of chronic urticaria patients and contrast to Sanjay et al study where drugs (19%) were major etiological factor and infections associated in 11% of patients.

It has been reported that CU is associated with various infections including bacterial, viral, parasitic and fungal. Bacterial infections (dental caries, tonsillitis, sinusitis, urinary tract infections) were found to be more common than parasitic infestations in the present study which is similar to Sanjay et al.

Dermographism is observed in 6% of CU patients which is in near agreement to studies done by Champion et al (8.5%) and Humphrey (9.5%).[15] Other forms of physical urticaria include cholinergic, contact, pressure and solar urticaria. Cholinergic urticaria is due to stimulation of postganglionic sympathetic nerves supplying sweat glands. Humphrey reported 1.28% of cholinergic urticaria, Champion et al reported 5.1% and Sanjay et al reported 7% of cholinergic urticaria where as in the present study it accounted for 2%.

Several recent reports indicate that contact allergy can also play a role in the etiopathogenesis of chronic urticaria. Guerra et al showed positive patch test to contact allergens in 41.3% of chronic urticaria patients.[16] In this study, contact allergy was elicited in 3% of CU patients. This parity may reflect the variation in the pattern of prevailing contact allergens in different places.

The reported incidence of CU patients due to the foods varies from 2 to 30% or more. More frequently implicated food additives like tartrazine, azodyes including amaranth and sunset yellow, benzoic acid compound, etc. An association of food and chronic urticaria was reported in 25% of cases by Singh et al and 17% cases by Sanjay et al which is nearer to the present study (21.7%). Diagnosing allergies to food is a compound process which further needs additional tests.

The association of drugs and chronic urticaria has been observed to vary from 6-10% in different studies. In the present series it was in 10.8% of the cases which is in agreement with Kozel et al.[17] Antibiotics (penicillin group) and NSAIDs are the common drugs responsible for aggravation of CU in this study.

Patients with autoimmune antibodies depend on ASST for clinical diagnosis as they have no specific diagnostic clinical features. Positive ASST gives a rough detection of histamine releasing propensity by mast cells and basophils in the patients with CIU. It is just suggestive of an autoimmune basis but not diagnostic.

Several studies were conducted to identify the incidence of AIU which is a subset of CIU and each study showed different results. Asero et al found the presence of autoantibodies in 67% patients but Kulthanan et al observed evidence of AIU in only 24.5% of CIU cases.[19,10]

In a similar way, several Indian studies also showed different varying results. Godse and George et al found 26.6% positive ASST and 34% positive ASST in CIU cases respectively.[6,13] Krupashankar and Verma et al found positive ASST results in 58.8% and 18% respectively.[20,21] In the present study, ASST was reported positive in 29.6% of CIU cases which is in concordance with the study done by Godse. The variation in the ASST results can be due to different sample size or due to procedure variation or parameter variation.

Limitations

The sample size of the study was small. The sensitivity of ASST is 70% and specificity is 80% having its own limitations. Histamine prick test as positive control is not performed due to risk of anaphylaxis and angioedema.

CONCLUSION

The etiology is not evident in many of chronic urticaria patients who were labelled as CIU. Infections followed by physical factors, food, and medication are the major etiological agents elicited. ASST is a cost-effective screening test for detecting patients with Autoimmune Urticaria who don't have definite clinical features differentiating them from CIU patients. ASST is important for the dermatologist in therapeutic point of view to initiate immunosuppressive therapy in autoimmune urticaria patients.

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Ethical approval: The study was approved by the institutional ethics committee

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