Research Article

Autologous serum skin test for evaluation of chronic idiopathic urticaria patients: a tertiary hospital study from central India

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Abstract

Background: Majority of patients with chronic urticaria, having no definite etiology are considered chronic idiopathic urticaria (CIU). In recent years, relatively significant number of chronic idiopathic urticaria patients has been classified as having autoimmunity on the basis of presence of auto antibodies (IgG anti IgE receptor alpha subunit or less frequently IgG anti IgE itself) which are responsible for mast cell and basophil activation. **Material and Methods:** A hospital based cross-sectional study was carried out in the Department of Skin, Chirayu Medical College and Hospital, Bhopal located in central India, during the period from August 2012 to February 2014 after institutional ethics committee approval. Total 53 Patients in the age range of 16 to 65 years of CIU were enrolled for study after detailed clinical history and physical examination. **Results:** Out of total 53 patients, 23(43.39%) showed wheal/ swelling of 1.5 mm or larger at test site as compared to that of control site, thus considered as ASST positive. Duration of CIU ranged from 4 months to 11 years with mean duration of 6.13±2.25 years**.** 19(82%) of the patients had lesions over whole body whereas only 4(17%) had lesions over face and limbs. 10(43%) patients had angioedema and 14(60%) had dermographism. **Conclusion:** ASST is simple, cheap and effective diagnostic method to detect presence of autoimmunity in CIU patients thus helps in identifying severity of disease and to choose appropriate therapeutic options accordingly. Our study did not elicit distinct clinical parameters of CIU (except number of wheals/ swelling and frequency of lesions, though statistically not significant) in ASST positive patients from those patients who didn't show ASST positivity.

Key words: Angioedema, Autologus Serum Skin Test, Chronic Urticaria, Chronic Idiopathic Urticaria

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Introduction

Urticaria is characterized by short-lived swelling of the skin due to transient leakage of plasma from small blood vessels into the surrounding tissue. Any pattern of recurrent urticarial wheals occurring twice weekly and persisting for longer than 6 weeks is called chronic urticaria(CU) [1]. Majority of patients with chronic urticaria, having no definite etiology are considered chronic idiopathic urticaria (CIU).

In recent years, relatively significant number of chronic idiopathic urticaria patients has been classified as having autoimmunity on the basis of presence of autoantibodies (IgG anti IgE receptor alpha subunit or less frequently IgG anti IgE itself) which are responsible for mast cell and basophil activation [2].

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Clinical and histological analysis of patients with CIU is generally insignificant to confirm its autoimmune origin. The most effective test to detect functional autoantibodies in chronic urticaria patients is basophil histamine release assay but proper standardization is lacking and its time consuming as well. Western blotting, enzyme-linked immunoabsorbent assay and flowcytometry using chimeric cell lines expressing the human FcRIα are the other options which may be useful in the future, however they still need to be validated [3]. Autologous serum skin test (ASST), on the other hand, is simpler and reasonable in-vivo intradermal test for measurement of histamine activity, released by basophilic degranulation, with high sensitivity of 70% and specificity of 80% [4, 5]. Therefore it is an effective diagnostic tool to detect presence of functional autoantibodies to FcεRIα and IgE and correlates with the disease activity and severity of clinical symptoms of CIU.

Present study was conducted to assess the usefulness of ASST positivity, in terms of its association with various clinical parameters of CIU, its impact on disease prognosis and planning therapy accordingly.

Material and Methods

It was a cross sectional study conducted in the department of dermatology, Chirayu Medical College and Hospital Bhopal, during the period from August 2012 to February 2014 after institutional ethics committee approval. Total 53 patients of CIU were enrolled for study after detailed clinical history and physical examination. Patients in the age range of 16 to 65 years were included in this study. Patients younger than 16 years and older than 65 years and pregnant/ lactating females were excluded from the study. Only those patients who had history of urticaria without specific cause/ etiology and persisting for longer than 6 weeks (as per CIU definition) before ASST were included in study. Written informed consent was taken from all enrolled patients after giving them complete information about the type and nature of the test, its usefulness and possible drawbacks.

All patients were advised to discontinue antihistaminic drugs for at least 3 days before the test. Each patient was interrogated about detailed clinical history of CIU (onset, duration, frequency, progression, severity etc), complete physical examination and relevant laboratory tests to exclude all possible causes of urticaria other than CIU.

Procedure

ASST was performed by storing 2 cubic centimeter of venous blood in sterile test tube and allowed to clot at room temperature for 30 minutes; then the serum was separated by centrifuging the blood at 2000 rpm for 10 minutes **(Figure no. 1)** Areas (e.g. forearm) devoid of any urticarial wheal/ swelling in last 24 hours were selected for test/ control site. 0.05 ml of autologous serum was injected intradermally into volar aspect of patient's forearm skin with 27G needle. Similarly same volume of normal saline (N.S.) was injected at control site; 5 cm away from test site (ASST site).Evaluation was done after 30 minutes. ASST was considered positive when diameter of test site (ASST site) wheal/swelling was found to be 1.5 mm or more than that of control (N.S.) site at the end of 30 minutes **(Figure no. 2).** It was considered negative when diameter of test site was found to be less than 1.5 mm **(Figure no. 3).** Wheal/ swelling diameter was measured as mean between the widest & perpendicular diameter.

Statistical Analysis

Data were entered in Excel sheet and statistical analysis was done by using Microsoft excel 2007.

Result

A total of 53 patients of CIU, including 20(37.73%) males and 33(62.26%) females were selected for the study with male to female ratio of 1:1.65, age range was 16-65 years with a mean of 33±8.2 years. Out of total 53 patients, 23(43.39%) showed wheal/ swelling of 1.5 mm or larger at test site as compared to that of control site; thus considered as ASST positive. Maximum number of patients showed ASST positivity in younger age group. Out of total 20 male patients,7(35%) were positive and out of total 30 female patients 16(48%) patients were positive for ASST, thus female preponderance (69.56%) of ASST positivity was observed in present study. Distribution of subjects according to age group, sex and ASST results was shown in **table no.1.**

Table No. 1: Distribution of subjects according to age group, sex and ASST results

Age group in years	Male(n=20)		Female(n=33)	
	ASST Positive N (%)	ASST Negative N (%)	ASST Positive N (%)	ASST Negative N (%)
16-25	2(10)	3(15)	7(21)	4(12)
26-35	1(05)	2(10)	3(09)	4(12)
36-45	2(10)	3(15)	1(03)	3(09)
46-55	1(05)	2(10)	3(09)	4(12)
56-65	1(05)	3(15)	2(06)	2(06)
Total	**07(35)**	**13(65)**	**16(48)**	**17(51)**

Out of total 53 patients, 23(43.39%) showed wheal/ swelling of 1.5 mm or larger at test site as compared to that of control site; thus considered as ASST positive. Maximum number of patients showed ASST positivity in younger age group. Out of total 20 male patients,7(35%) were positive and out of total 30 female patients 16(48%) patients were positive for ASST, thus female preponderance (69.56%) of ASST positivity was observed in present study.

Table No. 2: Distribution of subjects according to ASST results and clinical parameters

Clinical parameters	ASST Positive(n=23)	ASST Negative(n=30)
Duration of disease in years		
0-1	02(08)	04(13)
1-3	03(13)	02(06)
3-5	07(30)	09(30)
>5	11(47)	15(50)
Distribution of lesions		
Whole body	19(82)	23(76)
Face and limbs	04(17)	07(23)
Frequency of the lesions/weak		
<2	03(13)	11(37)
2-5	07(30)	14(46)
>5	13(56)	05(16)
Number of wheels		
0-10	02(08)	08(26)
11-20	06(26)	15(50)
>20	15(65)	07(23)
Size of the wheel in cm		
0-2	03(13)	05(16)
2-5	12(52)	15(50)
>5	08(34)	10(33)
Angioedema		
Present	10(43)	12(40)
Absent	13(56)	18(60)
Dermographism		
Present	14(60)	16(53)
Absent	09(39)	14(46)
Family history of atopy		
Present	08(35)	13(43)
Absent	15(65)	17(56)

Duration of disease : Duration of CIU ranged from 4 months to 11 years with mean duration of 6.13±2.25 years, Out of total 23 ASST positive patients, 2(8%) had duration of 0-1 year, 3(13%) had duration of 1-3 years, 7(30%) had duration of 3-5 years and 11(47%) had duration of >5years.

Distribution of the lesions: Out of total 23 ASST positive patients, 19(82%) of the patients had lesions over whole body whereas only 4(17%) had lesions over face and limbs. Distribution of lesions in ASST positive patients was comparable to that of ASST negative patients.

Frequency of lesions: 3(13%) out of total 23 ASST positive patients had frequency of wheal formation less than 2 times/ week. 7 (30%) had frequency of wheal formation 2-5 times/ week. 13 (56%) had frequency of more than 5 times/ week. This was in contrast to ASST negative patients where maximum number of patients (14, 46%) had 2-5 times wheel formation in a week.

Number of wheals: Maximum 15 (65%) of the patients in ASST positive group had history of more than 20 wheels over the body followed by 11-20 wheels in 6(26%) of the patients while maximum number of ASST negative patients had 11-20 wheels.

Size of wheels: Out of total 23 ASST positive patients, 12(52%) patients had wheel size between 2-5 cm, 8(34%) had wheel size more than 5 cm and only 3(13%) had wheel size less than 2 cm.

Angioedema and Dermographism: Out of total 23 ASST positive patients, 10(43%) patients had angioedema and 14(60%) had dermographism. Frequency of angioedema and dermographism was comparable in test and control group.

Family history of atopy: Out of total 23 ASST positive patients, family history of atopy was present in 8(35%) patients and absent in 15(65%) patients. Distribution of the patients according to the various clinical parameters and ASST results were shown in **table no.2.** None of patient developed/ complained any ASST testing induced adverse effect during or after procedure.

Discussion

Chronic urticaria (CU) is a common skin disease and can be disabling in its severe form. In approximately 70 to 90 % of patients with chronic urticaria, no definite etiology can be identified; such cases are categorized as chronic idiopathic urticaria (CIU). About half of patients of CIU show circulating IgG autoantibodies against high affinity IgE receptor or less commonly IgE itself followed by mast cell degranulation and release of histamine; therefore strongly suggest autoimmune variant of CU. This subset of urticaria has been shown to have relatively prolonged course of disease with poor response to conventional therapy. Besides detecting autoimmune basis, ASST helps in identifying amount of severity and prognosis of CIU as well as approaching specific therapeutic options.

Figure 5: Sample for ASST

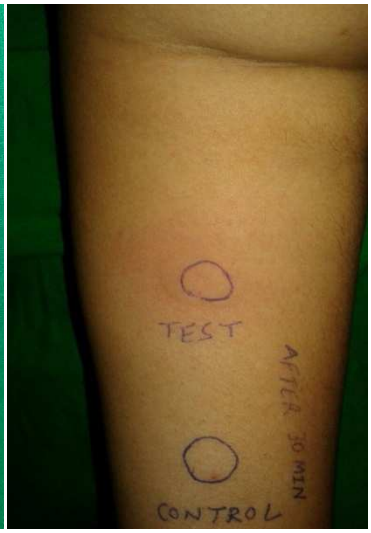

Figure 2: Positive ASST

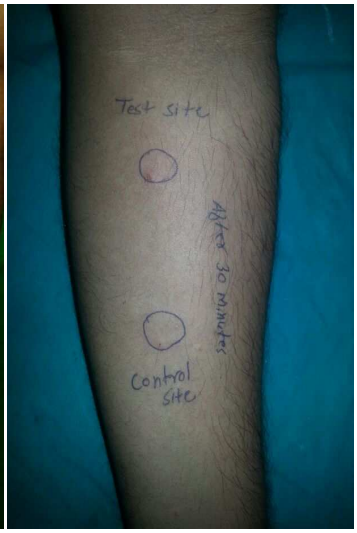

Figure 3: Negative ASST

In our study, highest number of patients showed ASST positivity in the age group of 16-25 years. Out of total 23 ASST positive patients, 7 were males who constituted 35% of total enrolled male patients, 30.43% of total ASST positive patients (irrespective of gender) and 13.20% of total study patients (irrespective of gender and ASST positivity) .16 ASST positive female patients demonstrated 48% of total female patients, 69.56% of total ASST positive patients (irrespective of gender) and 30.18% of total study patients (irrespective of gender and ASST positivity). Female preponderance of ASST positivity was observed whereas in another study conducted by George et al male to female ratio was found to be 1:1.2 with female preponderance [6].

Our study showed maximum ASST positivity in 11(47%) patients having the disease since more than 5 years, whereas in a study conducted by Jonathan Te- Peng Tseng et al in 2009, mean duration of disease was 1.36 years in ASST positive patients [7].

Out of total 23 ASST positive patients, 82% of the patients had urticarial lesions all over body, rest patients had lesions over face and limbs; similar findings were observed in a study conducted by Hayder R and Al Hamamy in 2013 [8]. There was no significant difference in ASST positive and negative patients in terms of distribution of lesions in present study. 56% ASST positive patients had frequency of wheel formation more than 5 times/ week. Similar findings regarding frequency of lesions were observed in a study conducted by Zeinab Abdel Azim and Shaymaa El Mongy in 2010 [9].

Out of ASST positive patients, maximum 15(65%) patients had history of more than 20 wheels over the body and 12(52%) patients had wheel size between 2-5 cm. In another study conducted by Kulthanan K and Jiamton S in 2006, 6 (28.6%) patients had more than 25 wheels on the body and 5 (23.8%) patients had wheel size more than 4cms [10]. 10(43%) ASST positive and 12(40%) ASST negative patients had angioedema, whereas in a study conducted by Verma et al in 2014, history of angioedema

was present in 54.5 % (109/200) patients and there was no statistically significant difference between ASST positive or negative patients [11]. There was no relation found in our study between results of ASST and presence of family history of atopy, atopic dermatitis or urticaria, similar findings were observed in a study conducted by Caproni M and Volpi W et al in 2004 [12].

Conclusion

ASST is simple, cheap and effective diagnostic method to detect presence of autoimmunity in CIU patients, thus helps in identifying severity of disease and choosing appropriate therapeutic options accordingly. Though ASST is an effective test to predict the presence of autoantibodies in CIU, positive ASST does not always mean autoimmune urticaria due to altered prevalence of ASST positivity in CIU as well as varied sensitivity and specificity from different studies. Our study did not elicit distinct clinical parameters of CIU (except number of wheals/ swelling and frequency of lesions, though statistically not significant) in ASST positive patients from those patients who didn't show ASST positivity.

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