

“Autologous Serum Skin Test in Chronic Urticaria”

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I. Introduction

Urticaria is a heterogenous group of diseases with presence of short lived, erythematous, edematous, cutaneous swellings secondary to transient dermal edema and vasodilatation¹. Angioedema (Quincke's edema) is a rapid swelling of the deeper dermis, subcutaneous tissue, mucosa and submucosal tissue².

Chronic urticaria is a distressing dermatosis characterized by spontaneous occurrence of wheals lasting for less than 24 hours, with or without angioedema occurring almost daily for more than 6 weeks.^{3,4} In many cases, the exact etiology remains unknown, hence they are categorized as chronic idiopathic urticaria (50%)³ or chronic spontaneous urticaria (CSU).⁵

However in a significant number of patients with chronic urticaria (30 – 50%), circulating histamine releasing functional autoantibodies directed against either high affinity IgE receptor (anti FcεR1a) on basophils and mast cells or less commonly against the immunoglobulin E (IgE) have been identified. Thereby the term chronic autoimmune urticaria has been assigned to these subgroup of patients.⁶

In rare cases, pseudo allergy (to salicylates, food, preservatives, antioxidants), infections (bowel parasites, H.pylori, intercurrent viral infections, candidiasis of bowel and chronic sepsis e.g. dental abscess), drugs (NSAIDs and aspirin, opioids, ACE inhibitors), psychological factors (anxiety, depression, impaired quality of life, significant discomfort in interpersonal relationships), and implants

(metal pin in the femur, metal dental prosthesis, dental amalgams. and nickel allergy), are implicated in chronic urticaria.² Overheating and local pressure of belts and clothing aggravates chronic urticaria and alcohol worsens urticaria by the mechanism of vasodilatation.⁷

Autologous serum skin test (ASST) is a simple in-vivo intradermal clinical test for the detection of histamine releasing activity.⁸ A positive result in the form of an immediate hypersensitivity reaction (read against a control) signifies the presence of circulating histamine releasing factors (autoantibodies).⁹ Hence ASST is an useful diagnostic aid in identifying chronic autoimmune urticaria. ASST has been found to have a sensitivity of approximately 70 % and a specificity of 80%.¹⁰ Though, basophil histamine release assay is the gold standard for detecting functional autoantibodies, the procedure is lengthy, requires fresh basophils from healthy donors and skilled expertise is desired.^{8,9}

Treatment of chronic urticaria possess a therapeutic challenge for the physician and a protracted, unsatisfactory deal for the patient. Moreover, patients experience restrictions in daily life activities and social life due to unrelenting symptoms, exhibit psychiatric co-morbidities, sexual difficulties, and reduced dermatology life quality index.¹¹

Identification of autoimmune urticaria may stimulate the use of immunotherapy in severe disease unresponsive to antihistamines. The present study is undertaken to study the clinical features of chronic idiopathic urticaria and correlate them with the result of autologous serum skin test.

II. Aims of the Study

1. To determine the incidence of positive autologous serum skin test in chronic idiopathic urticaria.
2. Comparison of clinical and laboratory parameters of patients with positive and negative Autologous Serum Skin Test.

III. Materials And Methods

In this present prospective observational study, 60 clinically diagnosed cases of chronic idiopathic urticaria attending the department of Dermatology, Venereology, Leprology at Prathima institute of medical sciences over a period of two years (2017 October – 2019 September) were enrolled.

Inclusion criteria:

All chronic idiopathic urticaria patients above 18 years, were examined after taking informed consent.

Exclusion criteria:

Pregnants, children below 18 years, urticaria secondary to physical causes, food and drugs, urticarial vasculitis were excluded.

Table – 1 URTICARIAL ACTIVITY SCORE4

SCORE	WHEELS	PRURITUS
0	None	None
1	Mild (<20 wheals/24hr)	Mild
2	Moderate (20-50 wheals/24hr)	Troublesome but does not interfere with sleep
3	Intense (>50wheals/24hrs of large confluent area of wheals)	Severe pruritus, which is sufficient troublesome to interfere with normal daily activity or sleep

MATERIALS USED:

1. Centrifuged serum of patient.
2. Sterile normal saline (0.9%)
3. 2 Insulin syringes.

Tests done for exclusion of physical urticaria included:

1. Symptomatic Dermographism – Moderate pressure was applied with back of pin traversing 10cm causing perceptible discomfort and reading was taken.
2. Cholinergic urticaria patient was made to exercise for 5-10 minutes until sweating and noted for development of wheals.
3. Localised heat urticaria : Test tube of hot water was placed on forearm for 10 minutes and observed for wheals at test site.
4. Cold urticaria: Ice cube in plastic bag was kept over forearm for 20 minutes. Reading was taken after 20 minutes.
5. Delay pressure urticaria – Weight of 7 kg was applied over the back for 15 minutes and observed for indurated lesion at test site after 6 hours.
6. Solar urticaria : Phototesting was done with solar simulator for solar urticaria using filters at 320 nm, 345 nm and 420nm for UV-B, UV-A and visible light respectively. Erythema and wheal at the test site indicated a positive reaction.

Laboratory investigations to exclude systemic causes included:

- Complete Blood Picture (CBP)
- Complete Urine Examination (CUE)
- Liver Function Test (LFT)
- Renal Function Tests (RFT)
- Thyroid Function Tests (TFT)
- Erythrocyte Sedimentation Rate
- Antinuclear Antibody (ANA)

Autologous Serum Skin Test (ASST)

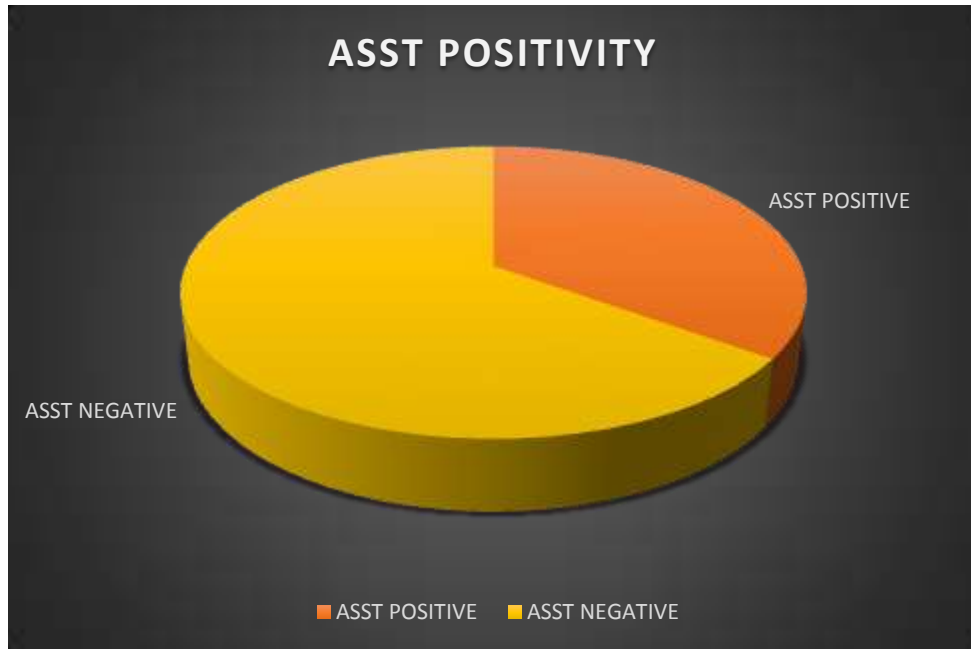


Positive ASST showing serum induced wheal 1.5 mm greater than normal saline wheal.

IV. Observation And Results

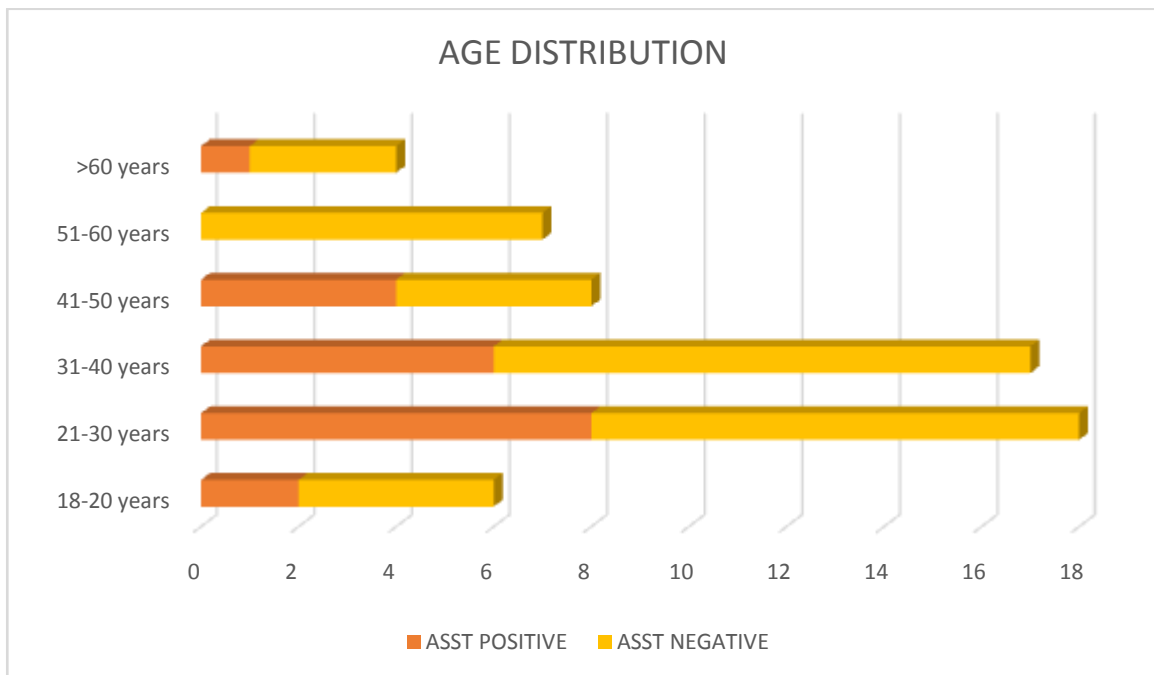
ASST POSITIVITY:

Among the 60 patients studied, ASST was positive in 21 (35%) patients and negative in 39 (65%) patients.



Age Distribution:

Maximum cases were in the age group of 21-30 years (30%), followed by 31-40 years (28.33%). The age of the youngest patient in this study was 18 years and that of the oldest was 80 years. The mean age at onset of urticaria in ASST positive patients was 35.31±13.85years, while it was 33.62 ±13.56 years in ASST negative patients.

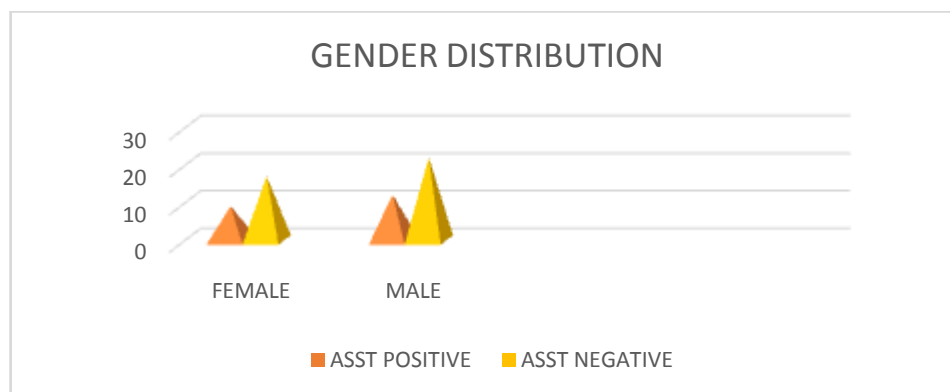


Sl.no.	Age group	ASST positive	ASST negative	Total patients	Percentage
1	18 – 20 years	2	4	6	10%
2	21 – 30 years	8	10	18	30%
3	31 – 40 years	6	11	17	28.33%

4	41 – 50 years	4	4	8	13.33%
5	51 – 60 years	0	7	7	11.66%
6	>60 years	1	3	4	6.66%

Gender Distribution:

Out of 60 patients 26 were females and 34 were males. ASST was positive in 9 (42.85%) out of 26 female patients and 12 (57.14%) out of 34 male patients.

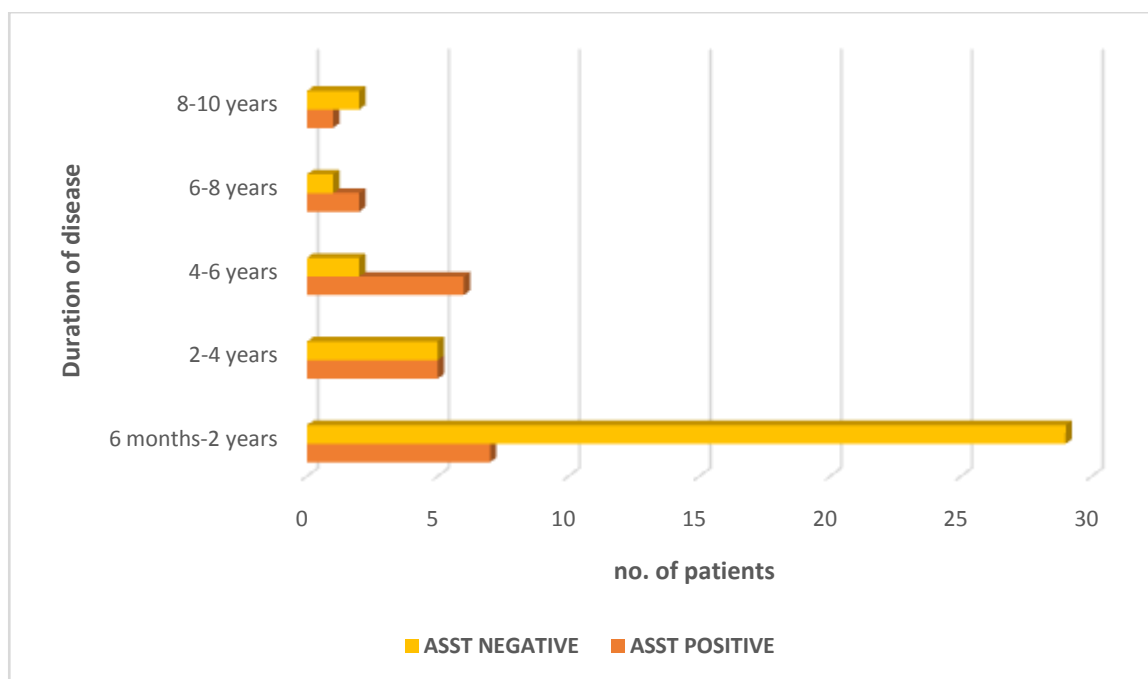


Sl.no.	Gender	ASST positive	ASST negative	P value
1	Male	9 (42.85%)	17 (43.58%)	0.116
2	Female	12 (57.14%)	22 (56.41%)	0.08

Duration of the disease:

The mean duration of the disease in ASST positive patients was 36.71 ± 34.62 months and 32.58 ± 29.49 months in ASST negative patients. In the present study the duration of disease in ASST positive patients were long lasting as compared to ASST negative patients.

Sl.no.	Duration of disease	ASST positive	ASST negative
1	6months – 2 years	7	29
2	2 – 4 years	5	5
3	4 – 6 years	6	2
4	6 – 8 years	2	1
5	8 – 10 years	1	2

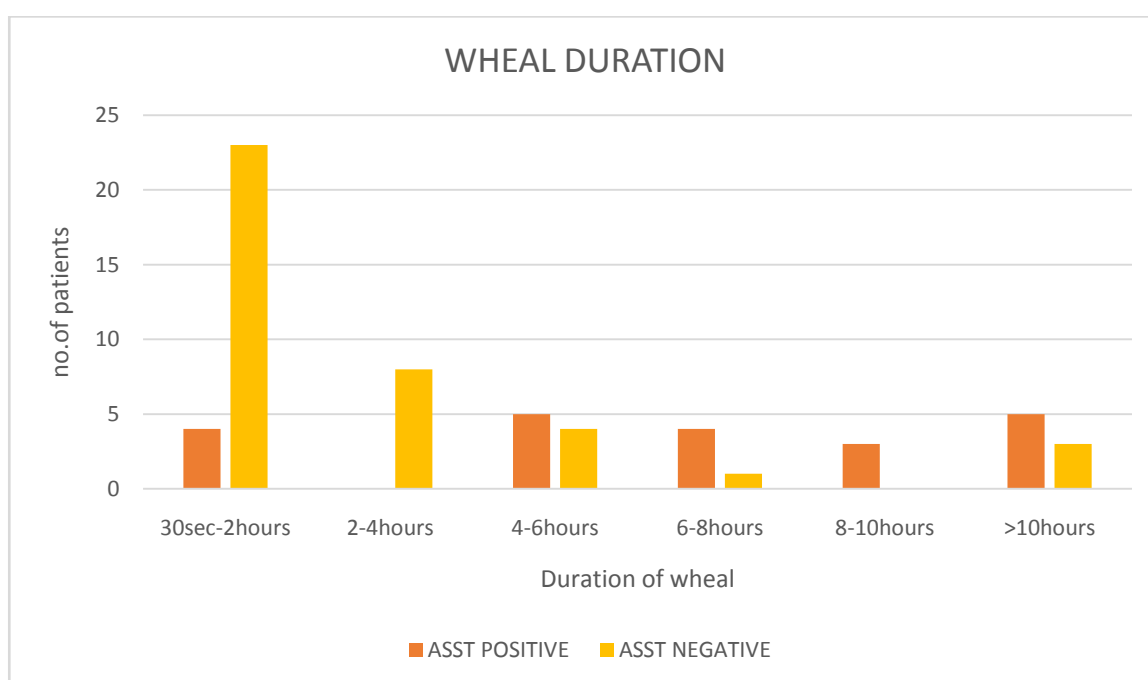


Duration of the wheal:

The mean duration of the wheal in ASST positive patients was 7.95 ± 4.42 hours and 3.33 ± 3.56 hours in ASST negative patients.

In the present study the duration of wheal in ASST positive patients were long lasting as compared to ASST negative patients.

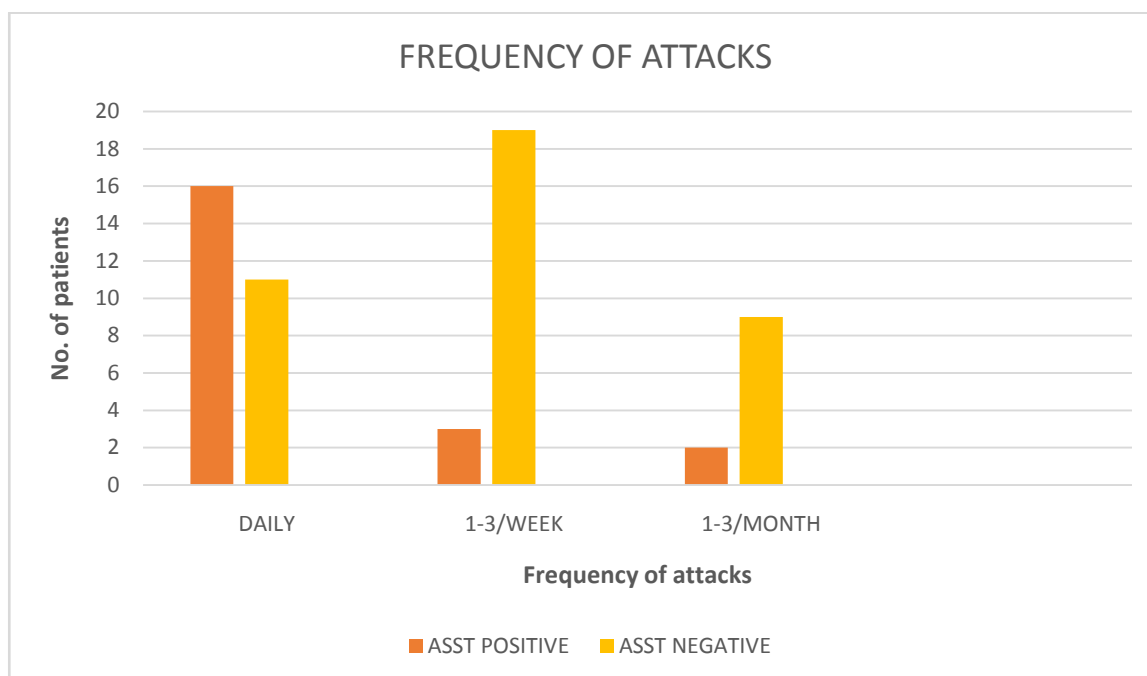
Sl.no.	Wheal duration	ASST positive	ASST negative
1	30sec – 2 hours	4	23
2	2-4 hours	0	8
3	4-6 hours	5	4
4	6-8 hours	4	1
5	8-10 hours	3	0
6	>10 hours	5	3



Frequency of attacks:

In the present study the attacks of urticaria were more frequent in ASST positive patients when compared to ASST negative patients. The percentage of patients having 1-3 attacks per week were 14.28% in ASST positive and 48.71% in ASST negative patients. The percentage of patients showing in 1-3 urticarial attacks per month were 9.52% in ASST positive and 23.07% in ASST negative patients.

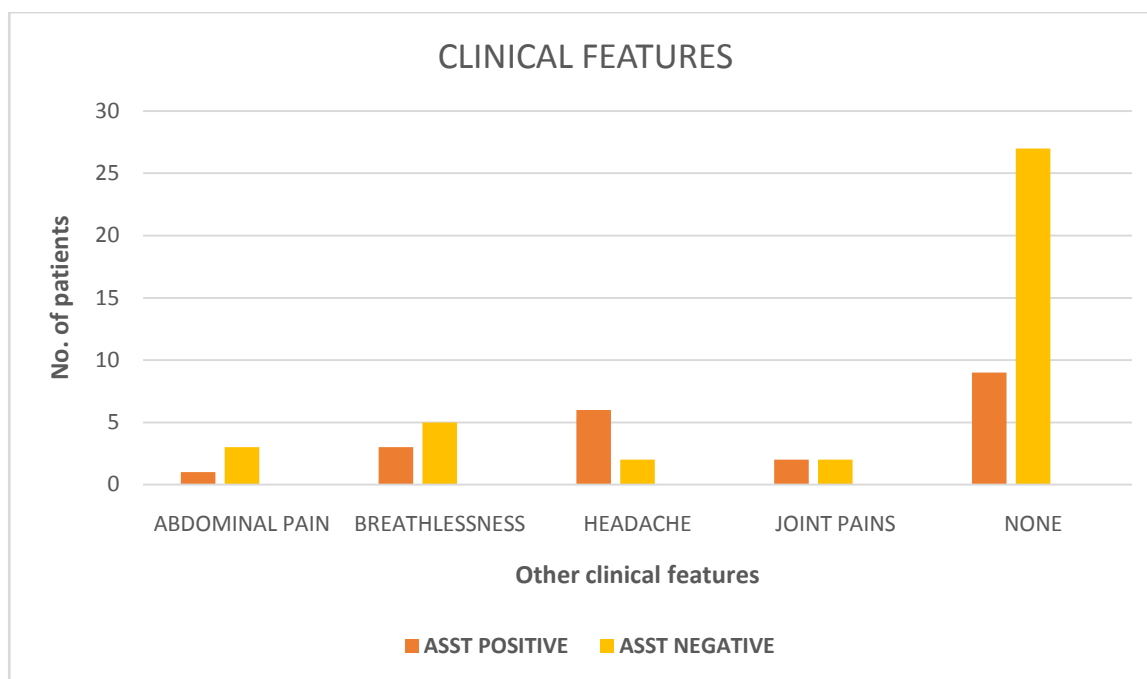
Sl.no.	Frequency of attacks	ASST positive	ASST negative	P value
1	Daily	16 (76.19%)	11 (28.20%)	0.00037*
2	1-3/week	3 (14.28%)	19 (48.71%)	0.0082*
3	1-3/month	2 (9.52%)	9 (23.07%)	0.195



Clinical features:

Different clinical features were compared like headache, joint pains, breathlessness, and abdominal pain. 27 (69.23%) out of 39 ASST negative patients did not had any other associated clinical features. Whereas 12 (57.13%) out of 21 ASST positive patients complained of various clinical features, among which 6 (28.57%) suffered with Headache. However such associations were statistically insignificant

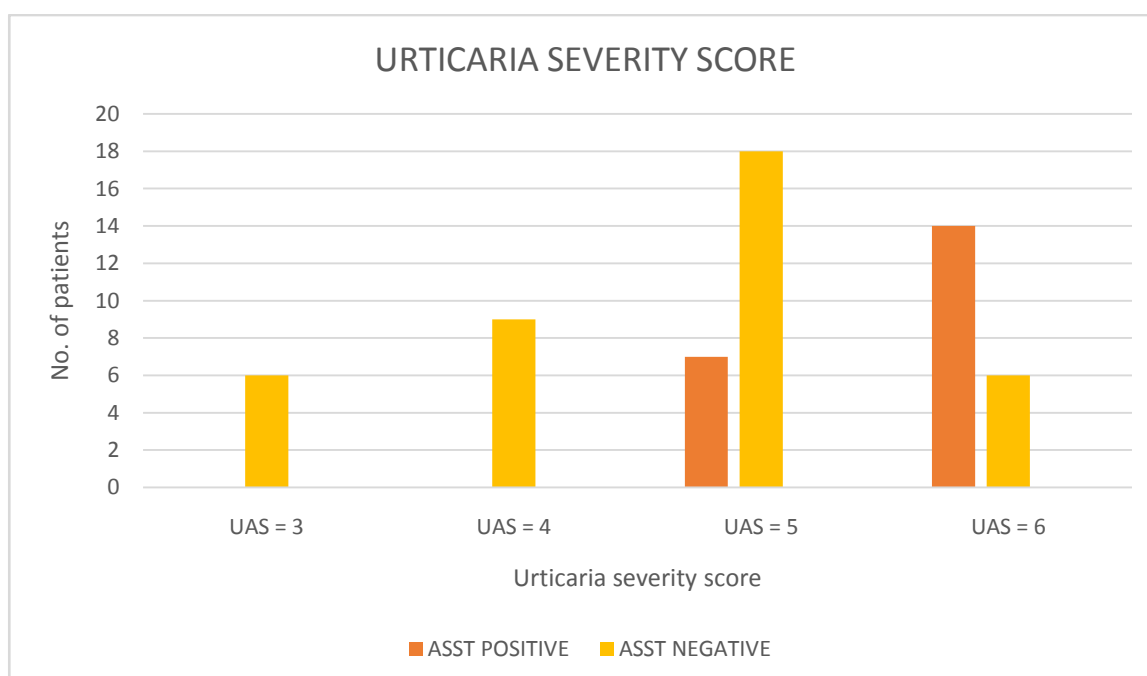
Sl.no.	Clinical features	ASST positive	ASST negative	P value
1	Abdominal pain	1 (4.76%)	3 (7.69%)	0.31
2	Breathlessness	3 (14.28%)	5 (12.82%)	0.47
3	Headache	6 (28.57%)	2 (5.12%)	0.15
4	Joint pains	2 (9.52%)	2 (5.12%)	1
5	Absent	9 (42.85%)	27 (69.23%)	0.0027*



Urticarial activity score:

Urticarial Activity Score is >4 in all the ASST positive patients as compared to ASST negative patients, which is statistically significant.

Sl.no.	UAS	ASST positive	ASST negative	P value
1	3	0	6 (15.38%)	0.014*
2	4	0	9 (23.07%)	0.0027*
3	5	7 (33.33%)	18 (46.15%)	0.0027*
4	6	14 (66.66%)	6 (15.38%)	0.736



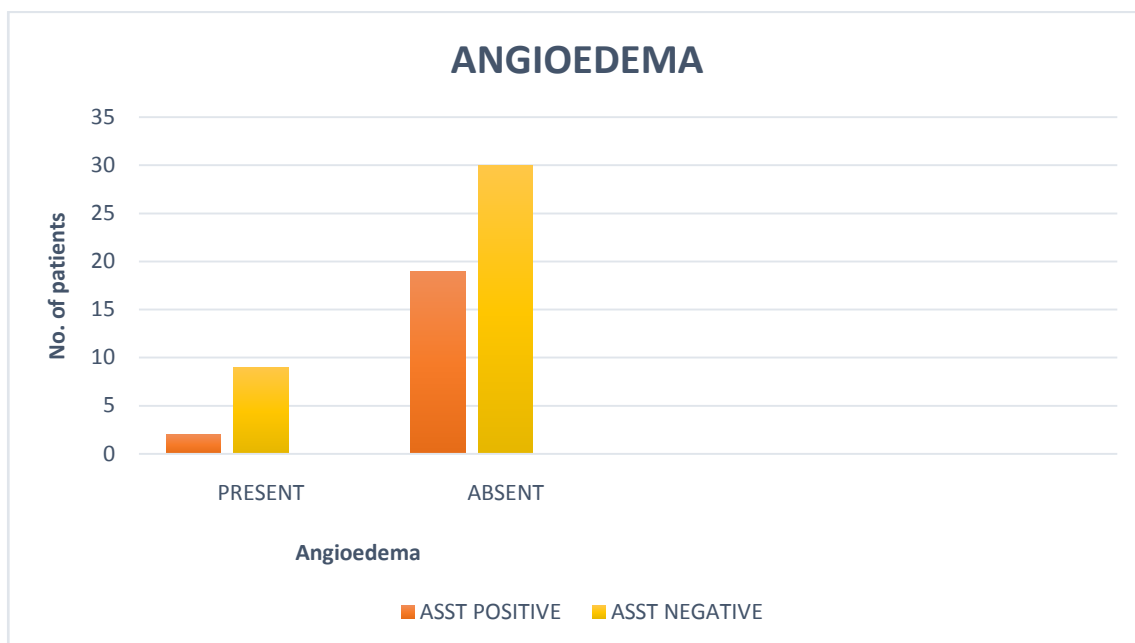
Dermographism:

Dermographism was present in 4.76% of ASST positive patients and 7.69% of negative patients, which was statistically not significant.

Sl.no.	Dermographism	ASST positive	ASST negative	P value
1	Present	1 (4.76%)	3 (7.69%)	0.31
2	Absent	29 (95.23%)	36 (92.30%)	0.032*

Angioedema:

Angioedema occurred in 9.52% of ASST positive patients and 23.07% in ASST negative patients. So it is significant in ASST negative patients.



Sl.no.	Angioedema	ASST positive	ASST negative	P value
1	Present	2 (9.52%)	9 (23.07%)	0.034*
2	Absent	19 (90.47%)	30 (76.92%)	

Medical illness:

Diabetes-I was present in 4.76% of ASST positive patients, while Diabetes – II is seen in 4.76% of ASST positive patients and 25.64% of ASST negative patients. Hypothyroidism is seen in 28.57% of ASST positive patients and 10.25% of ASST negative patients.

Sl.no.	Medical illness	ASST positive	ASST negative
1	Absent	13 (61.90%)	25 (64.10%)
2	Diabetes 1	1 (4.76%)	0
3	Diabetes 2	1 (4.76%)	10 (25.64%)
4	Thyroid	6 (28.57%)	4 (10.25%)

Complete blood picture :

Anaemia and leucocytosis were seen in 19.04% & 4.76% of ASST positive patients and 10.25% & 7.69% of ASST negative patients. Both the values were insignificant.

Sl.no.	CBP	ASST positive	ASST negative
1	Anemia	4 (19.04%)	4 (10.25%)
2	Leucocytosis	1 (4.76%)	3 (7.69%)
3	Normal	16 (76.19%)	32 (82.05%)

Absolute eosinophil count:

AEC was raised in 9.52% of ASST positive patients and 17.94% of ASST negative patients, which was insignificant.

Sl.no.	AEC	ASST positive	ASST negative	P value
1	Normal	19 (90.47%)	32 (82.05%)	0.0083
2	Raised	2 (9.52%)	7 (17.94%)	0.0955

Erythrocyte sedimentation rate:

ESR was normal in all ASST positive patients, whereas it was raised in 10.25% of ASST negative patients, but these results were insignificant.

Sl.no.	ESR	ASST positive	ASST negative	P value
1	Normal	21 (100%)	35 (89.74%)	0.0163
2	Raised	0	4 (10.25%)	0.045

Thyroid profile:

Thyroid profile was abnormal in 33.33% of ASST positive patients and 15.38% of ASST negative patients. Statistically these results were insignificant.

Sl.no.	Thyroid profile	ASST positive	ASST negative	P value
1	Normal	14 (66.66%)	33 (84.61%)	0.005
2	Abnormal	7 (33.33%)	6 (15.38%)	0.78

ANA profile:

ANA profile abnormality was noticed in 2.56% of ASST negative patients. None of the ASST positive patients showed abnormal ANA profile.

Sl.no.	ANA profile	ASST positive	ASST negative	P value
1	Normal	100%	38 (97.43%)	
2	Abnormal	0	1 (4.76%)	0.317

V. Discussion

Chronic Urticaria is rarely life threatening but wide spread urticaria and its associated angioedema can be both debilitating and frightening. Approximately 15-20% of the population may experience at least one episode of urticaria in their lifetime and about one quarter of these patients are likely to develop chronic urticaria.¹⁰

The challenge for the clinician is to try and identify a cause that could lead to a specific treatment or avoidance strategy.¹²

The basophil histamine release assay is currently the gold standard for detecting these functional auto-antibodies in the serum of patients with chronic urticaria.

However, this bioassay is difficult to standardize because it requires fresh basophils from healthy donors, is time-consuming and it remains confined to research centres. Other useful screening tools are Western blot, ELISA and flow cytometry, but are yet to be validated.

ASST is simple, semi-invasive, inexpensive, easy to perform and Results can be obtained within 30 minutes. Hence it is the best in vivo clinical test for detection of basophil histamine releasing activity

Percentage of ASST positivity :

In the present study ASST was positive in 21 (35%) patients and negative in 39 (65%) patients. The percentage of ASST positivity in various other studies is as follows :

Study	ASST positivity
Vohra et al ⁸	46%
Vikram kumar et al ⁹	41.6%
Hayder et al ¹³	40.7%
Mamata et al ¹⁴	34%
Azim et al ¹⁵	21.7%

Safari et al ¹⁶	39%
Boopiyathad et al ¹⁷	37%
Noha et al ¹⁸	40%
Sajedi et al ¹⁹	65.5%
Krupashankar et al ²⁰	51.1%

Italian patients with CIU showed a positive ASST in 67%.²¹ where as it was 26.67% In Indian population⁸, 24.7% among Thai patients.²² The prevalence difference among various ethnic groups suggests a genetic background for the disease.

Age distribution of the patients :

In the present study, CIU was found to be more common among the age group of 21-30 years (30%), followed by 31-40 years (28.33%) and 41-50 years.

Study	Age distribution
Vohra et al ⁸	32.69 ± 13 years
Hayder et al ¹³	32 ± 11.7 years
Azim ZA et al ¹⁵	34.3 ± 10.2 years
Yadav et al ²³	32.5 years
Krupashankar et al ²⁰	20-30 years

All the above studies shows that chronic idiopathic urticaria is common among the reproductive age group, these results were consistent with the present study. There is no statistical significance pertaining to the age group between ASST positive and negative groups, these results were also consistent with the present study.

Gender distribution :

In the present study, out of 60 patients 26 were females and 34 were males. ASST was positive in 9 out of 26 (42.85%) female patients and 12 out of 34 (57.14%) male patients.

Studies by Hayder et al¹³, Mamata et al¹⁴ and Krupashankar et al²⁰ showed that the sex of the studied population did not affect the positivity of ASST.¹³

Whereas in studies by Azim ZA et al¹⁵ & Vohra et al,⁸ they showed that females outnumbered the number of males among the ASST – positive patients. The present study correlates with the same.

Duration of the disease:

In the present study the mean duration of the disease in ASST positive patients is 36.71 ± 34.62 months and 32.58 ± 29.49 in ASST negative.

Various studies by Vohra et al,⁸ Hayder et al,¹³ Mamatha et al,¹⁴ found that duration of disease did not influence the positivity of ASST .

Duration of the disease was significantly longer, in patients with positive ASST than in patients with negative ASST in studies done by Sabroe et al¹⁰ and by Azim et

al.¹⁵ A significant increase (p=0.002) in the duration of the disease in ASST positive group (median 4 years) in comparison to that of ASST negative group (median 1 year) was observed by Azim ZA et al.¹⁵ These results were in concordance with the present results.

Duration of wheal:

The mean duration of the wheal in ASST positive patients is 7.95 ± 4.42 hours and 3.33 ± 3.56 hours in ASST negative patients. P value is 0.000, which is highly significant.

Mamatha et al. Observed that Wheals lasted for significantly longer duration in patients with positive ASST. The median duration being four hours for ASST positive patients compared to two hours in ASST-negative individuals (P=0.001,

Mann-Whitney Test), which was statistically significant.¹⁴

These results were consistent with the present study.

Krupashanker et al study reported that the duration of each attack varied from minimum of half-an-hour to a maximum of more than 12 hours but less than 24 hours. The average duration of each urticarial attack lasted for about 6.5 hours. In 53.75% of the patients, each attack of urticaria lasted for about 6-12 hours.²⁰

Frequency of attacks:

Patients with ASST positivity were seen to experience more frequent attacks of urticaria on daily basis when compared to ASST negative patients. Of the Total patients presenting with 1-3 attacks per week 14.28% were ASST positive and 48.71% were ASST negative. The percentage of patients showing in 1-3 urticarial attacks per month were 9.52% ASST positive and 23.07% ASST negative.

In studies by Hayder et al and Krupashankar et al, there was no significant relation between positivity of ASST and frequency of attacks. These results were not consistent with the present study.^{13,20}

In various other studies, by Vohra et al⁸, Mamata et al¹⁴, and Azim ZA et al¹⁵ patients with positive ASST had more frequent attacks when compared to ASST negative group.

These results were consistent with the present study.

Clinical features:

According to our study ASST positive patients had associated clinical features more frequently than ASST negative patients. 27 (69.23%) out of 39 ASST negative patients did not had any other associated clinical features. Whereas 12 (57.13%) out of 21 ASST positive patients complained of various clinical features, among which 6 (28.57%) suffered with Headache. However such associations were statistically insignificant. Similar results were noted in other studies as well.

Vohra et al⁸ study shows that Multiple symptoms were associated in 24 (52%) ASST-positive and 20 (37%) ASST negative patients respectively. The gastrointestinal symptoms like abdominal pain, diarrhoea, indigestion (13 patients), general malaise, headache, loss of concentration, lassitude, feverish feel and feeling of hot or cold (45 patients), breathlessness/wheezing, palpitations (12 patients) and joint pains (two patients) were more frequent in the ASST-positive cases while symptoms like nausea/vomiting (three patients), flushing (seven patients), joint swelling (one patient) and syncope (three patients) were seen more often in those with negative ASST. However, the difference was not statistically significant (P = 0.18).⁸

ASST-positive patients had significantly more systemic symptoms in a study by Juhlin et al particularly, gastrointestinal symptoms and flushing occur more frequently in patients with autoantibodies.²⁴

In study by Krupa shanker et al²⁰ 33 patients out of 80 had other associated conditions. Out of which, headache was the commonest, which was seen in 17 (21.25%) patients, followed by white discharge per vagina in 7 (8.75%), throat pain in 7 (8.75%), sinusitis in 5 (5.46%), abdominal pain in 5 (5.46%), vomiting in 3 (3.75%), fever in 3 (3.75%), diarrhoea in 3 (3.75%), urinary tract infection in 2 (2.5%), and rheumatoid arthritis in 1 (1.25%), but it does not reveal any statistical significance among ASST positive and negative groups.

Urticarial activity score:

In the present study Urticarial Activity Score is >4 in all ASST positive patients as compared to ASST negative patients, which is statistically significant.

Severity of urticaria, as measured by UAS, was significantly higher in ASST positive group compared to ASST negative group. Both Sabroe et al²⁵ and Caproni et al.²⁶ also found that patients with positive ASST presented more severe clinical features than those with negative ASST. These results were consistent with the study.

However, Nettis et al.²⁷ stated that there was insignificant difference between the two groups regarding UAS.

Where as In Hayder et al¹³ study the severity score was divided into three groups: mild (upto 5), moderate (6-10), and severe (>10) and their relation to the positivity of ASST was found to be not significant (P value 0.406). These results were not consistent with the present study.

Dermographism:

In the present study dermographism was present in the 4.76% of ASST positive patients and 7.69% of negative patients, which was statistically not significant.

Azim ZA et al¹⁵ study observed that 80% of ASST positive patients show dermographism, while 60% in the ASST negative group, This does not show any statistical significance.

Dermographic subjects comprise a special group. They do not have autoantibodies according to in vitro tests but manipulation of skin while injecting the sample may cause a wheal and flare response regardless of the substance injected and may be taken as false positive responses.¹⁰

Angioedema:

According to the current study angioedema is present in 9.52% ASST positive patients and 23.07% in ASST negative patients. So it is statistically significant in the ASST negative patients.

In the study group of Krupa Shanker et al.²⁰ angioedema was present in 27.3% of ASST negative patients and 51.1% of ASST positive patients, which was statistically significant.

These results were not consistent with the present study.

However, the observations of Nettis et al.²⁷ that the prevalence (69%) of angioedema is significantly higher in the ASST-positive cases as compared with that (43%) in the ASST-negative patients.

Swerd et al.²⁸ observed angioedema in 86% of the ASST-positive and 67% of the ASST-negative patients, which was not statistically significant.

In Mamatha, et al.¹⁴ study Angioedema occurred in 15 out of 100 patients. In a similar study done by Sabroe et al. angioedema occurred in 93 out of 107 cases. In both these studies, there was no significant difference between ASST-positive or negative patients in the incidence, duration, frequency or distribution of angioedema. In Hayder et al.¹³ study there was no relation between results of ASST and the presence of angioedema (P-value 0.641),

According to Azim ZA, et al.¹⁵ study angioedema was present in 46.7% of ASST positive patients and 40% of ASST negative patients. There was insignificant difference between ASST positive and negative groups regarding angioedema association. This finding was in agreement with that reported by Kulthanan et al.²⁹

These results were inconsistent with the present study.

Vohra et al.⁸ observed ASST-positive and ASST negative patients, respectively, but both groups were comparable in the number of episodes (total 1 to >50) and the sites involved (lips, eyelids, buccal mucosa or tongue, hands and feet). In the ASST-positive patients, involvement of throat was significantly higher (P<0.04) when compared with that in the ASST-negative patients.

The present study could not explain the sites of involvement of angioedema.

Medical illness:

Autoimmune diseases like thyroid disease, vitiligo, diabetes mellitus, pernicious anaemia, and rheumatoid arthritis were reported more commonly in patients with autoimmune urticaria.³⁰

Hayder et al. found no relation between the autoimmune diseases like thyroid, diabetes mellitus, vitiligo, and rheumatoid disease (p-value 0.079).¹³

Mamatha, et al. study did not find an increased incidence of other autoimmune diseases.¹⁴

Krupa shanker et al.²⁰ study observed that diabetes mellitus was seen in 5 (6.3%) patients, 2 (2.5%) were hypothyroid, but no statistical correlation was observed.

These results were consistent with the present study.

CBP:

In the present study anaemia was present in 19.04% of ASST positive patients and 10.25% of ASST negative patients. Leucocytosis is present in 4.76% of the ASST positive patients and 7.69% of ASST negative patients. Statistical difference was not found regarding abnormal CBP.

Pernicious anaemia is an important factor to rule out autoimmunity as a causative factor for autoimmune urticaria.

Krupa shanker et al.²⁰ observed that Level of haemoglobin was low in 3.1% of ASST negative patients and 6.4% in ASST positive patients. Insignificant p value was observed between ASST positive and negative groups. These results were consistent with the present study.

Krupa Shanker et al. study found that leucocytosis was present in the 12.14 of the ASST negative patients and none of them with ASST positive. These results were statistically significant.²⁰

The above results were not consistent with the present study.

Absolute eosinophil count:

In the present study absolute eosinophil count was raised in 9.52% of ASST positive patients and 17.94% of ASST negative patients. This was not statistically significant.

Krupa shanker et al. study observed that raised AEC was seen in 12.1% of ASST negative patients and 8.5% of ASST positive patients, which is not statistically significant.²⁰

These results were consistent with the present study.

Whereas Azim ZA et al. study observed that peripheral blood absolute eosinophil count was raised in ASST positive group (mean \pm S.D ;176.6 \pm 57.2/mm³) in comparison to ASST negative group (mean \pm S.D; 176.6 \pm 57.2/mm³) . It was statistically significant.¹⁵

Although blood eosinophil count was significantly higher in ASST positive group than in ASST negative group, the level in both groups was below the upper normal value. The reduction in blood eosinophil count in CIU is consistent with their: presence in lesional skin biopsy.²⁵ The role of tissue eosinophilia is unclear, but it is possible that release of toxic eosinophil major basic protein and eosinophil cationic protein further augments histamine release from mast cells in the late phase of urticaria. These results were not consistent with the present study.

Erythrocyte sedimentation rate:

In the present study ESR was raised only in ASST negative patients. However, Krupa Shanker et al. study observed that ESR was raised in 6.1% of ASST negative patients and 6.4% of ASST positive patients, which was not significant.²⁰ This study results were not consistent with present study.

Thyroid profile:

Thyroid abnormality was present in 33.33% of ASST positive patients and 15.38% of ASST negative patients. These results were not significant. Mamatha, et al observed abnormal TFT values in three ASST-positive patients. This study did not find any difference in the incidence of thyroid disease.¹⁴ The above results were consistent with the present study. Leznoff et al.³¹ postulated that thyroid autoimmunity may play a role in the pathogenesis of chronic urticaria and angioedema. Krupa shanker et al²⁰ study did not find significant difference of thyroid profile among the ASST positive and ASST negative groups. The above study results were similar to the results of present study. This study did not find any difference in the incidence of thyroid disease. This is likely because an insufficient number of patients were included for the study of a disease of low incidence (thyroid autoimmunity) or because TFT and thyroid autoantibodies were not routinely measured for all patients. Thus, TFT alone is not enough to rule out thyroid disease and the thyroid antibody test should be carried out in all chronic idiopathic urticarial patients.

ANA profile:

ANA profile was positive only in one patient with ASST negative, which is statistically insignificant. Mamatha, et al study showed, of the ten patients tested, ANA was positive in one patient who also had positive ASST. This study did not find an increased incidence of other autoimmune diseases.¹⁴ O’ Donnel et al. Study found a higher frequency of autoimmune disease in patients with autoimmune urticaria.³² Krupa Shanker et al²⁰ study observed patients with ASST positive did not show any significance with H. pylori antibodies, thyroid antibodies, ANA. There are also a few reports suggesting an association specifically between ASST positive CU patients and ANA positivity.³³

COMPARISON WITH VARIOUS STUDIES

TABLE-17

Authors	Sabroe et al.	George et al.	Vohra et al.	Krupa Shankar et al.	Present study
Mean age of presentation	45	34	14-63	14-75	18-80
Male / female ratio	88/19	44/56	31/69	36/44	34/26
% of patients with autoimmunity	31%	34%	46%	58.8%	35%

Correlation of frequency and positive ASST	Present	Present	Present	Present	Present
Correlation of duration and positive ASST	Present	Present	Present	Present	Present
Angioedema	93/107	15/100	55/100	33/80	11/60
Correlation of systemic symptoms and positive ASST	Present	No	No	No	No
Thyroid disease	No	No	No	No	No

In the present study, different parameters like age, gender, urticaria severity score, duration of disease, duration of wheals, frequency of attacks per week, interference with daily activities and sleep, presence of angioedema and associated autoimmune diseases were studied to evaluate any proposed relationship between these parameters and the positivity of the ASST.

Statistical analysis of these patients did show a significant difference between patients with positive and negative ASST for frequency of attacks, urticaria severity score, duration of each wheal and duration of disease.

In agreement with present study observations, other studies found that patients with autoantibodies in their sera (CIU, who have positive ASST results) have distinctive diagnostic clinical features that differentiate them from patients who do not have these antibodies (CIU, who have negative ASST results).

ADVANTAGES:

ASST is simple, cost-effective test for detecting CAU patients who have no distinctive clinical features differentiating them from CIU patients.

LIMITATIONS OF THE PRESENT STUDY:

- I. ASST has a sensitivity of approximately 70% and a specificity of 80%, so ASST itself has its own limitations.
- II. Skin prick test with histamine diphosphate as positive control is not performed due to risk of anaphylaxis and angioedema.
- III. The study has not determined how many patients in particular groups showed symptoms associated with the hypersensitivity to pseudo allergens which may be seen in few patients.
- IV. The present study did not determine the concurrent presence of Hashimoto’s disease or anti-thyroid antibodies, which may contribute to intensification of the symptoms in some ASST-positive cases.
- V. The present study fails to explain the sites of involvement of angioedema and urticaria.

VI. Summary

A total of 60 consecutive cases of chronic idiopathic urticaria reporting to the Dermatology Venereology Leprology department of Prathima hospital were studied. 26 of them were females and 34 were males. The age group of 21-30 years (30%) outnumbered the rest. The age of the youngest patient was 18 years and that of the oldest was 80.

- 1) Autoantibodies, as detected by ASST, were seen in the sera of 35% patients with CIU, comparable to available reports in literature.
- 2) Presence of these autoantibodies was significantly associated with more frequent attacks, urticaria severity score, duration of each wheal and duration of disease.
- 3) Presence of autoantibodies was unrelated to age and sex.
- 4) Angioedema was significant in ASST negative patients.
- 5) There was no correlation or trend towards correlation between ASST positivity and other autoimmune disorders tested i.e., Thyroid dysfunction and ANA.
- 6) There was difference in CBP, AEC, ESR, Thyroid, ANA between positive and negative ASST patients, but these results were statistically insignificant.

VII. Conclusion

ASST is a simple screening test and cost-effective test for detecting CAU patients who have no distinctive clinical features differentiating from CIU patients. ASST also identifies a sub group of patients with CIU with more severe disease, who are likely to be more symptomatic and would require more aggressive treatment.

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PICTURES



Urticarial wheals



Angioedema

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