



To study the association of chronic spontaneous urticaria with anti thyroid peroxidase antibody and ASST

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Abstract

Background: *Urticaria is a disease with weals and itching seen in all age groups. It can be acute or chronic, and chronic can be further subdivided into chronic inducible urticaria and chronic spontaneous urticaria.*

Till date some many antibodies have been found to be associated with chronic spontaneous urticaria. Autologous serum sensitivity test has emerged as one of the invasive investigations being tried in detecting the autoimmune nature of the disease.

Through this study, we are trying to find out the association of antithyroid peroxidase antibody (anti TPO) with CSU (chronic spontaneous urticaria) and correlate the severity of CSU with ASST positivity.

Objectives: *To find out if there is any association of chronic autoimmune urticaria with anti TPO and ASST to correlate its severity with them.*

Method: *Ours was a crosssectional study whereby we have investigated all the enrolled patients for anti TPO and performed ASST on them. A total of 137 consecutive patients were enrolled and investigated for serum anti TPO and ASST performed on them. The datas were analysed using SPSS software 2019 version.*

Result: *In this study anti TPO antibodies and ASST was found to be positive in patients of CSU .While anti TPO has come out to be a screening tool and ASST a better diagnostic tool.*

Conclusion: *We can conclude from the study that CSU is associated with anti TPO.*

Keywords: *CSU, Anti TPO, ASST, association.*

Introduction

Chronic urticaria (CU) is defined by the presence of recurrent urticaria (hives), with or without angioedema, for a period of six weeks or longer^(1,2). As many as 40-50 percent of patients with CU have accompanying episodes of angioedema⁽²⁾. No external allergic cause or contributing disease process can be identified in

80 to 90 percent of adults and children with CU. There are several theories regarding the pathogenesis of chronic idiopathic urticaria (CIU) or chronic spontaneous urticaria (CSU), none of which have been conclusively established. CU is a self-limited disorder in most patients, although the average duration of disease is two to five years.⁽³⁻

⁵⁾ The first indications that CU might have an

autoimmune origin were noted by Leznoff et al who suggested that there is an increased incidence of antithyroid antibodies (antimicrosomal and antithyroglobulin) in approximately 12% to 15% of such patients.^(3,4) The autoimmune subgroup of chronic urticaria has shown association with antithyroid antibodies.⁽⁶⁾ The pathogenesis suggested till date is the presence of IgG antibody to the alpha subunit of the IgE receptor in 35-40% cases of CSU.⁽⁷⁾ Further these antibodies have been found to be usually reactive with unoccupied IgE receptors or IgG Ab to IgE in 5-10% & the IgG subclass most commonly found to be pathogenic in cases of CSU are IgG(1) & IgG⁽³⁾⁽⁸⁾. Presently, ASST is one of the most useful tests for confirming a diagnosis of chronic autoimmune urticaria with sensitivity & specificity respectively of 65–81% & 71–78%⁽⁹⁾. Basophils being an important factor in the pathogenesis of CSU, the basophil activation test can be a useful screening tool for confirmation of autoimmune basis of the disease but further confirmatory studies are needed for its acceptance.⁽¹⁰⁾ Here comes the role of ASST which though invasive can be a useful tool for confirming a case of CSU as CAU. Not only this, ASST positive patients are seen to have a severe course of disease thereby requiring high dose of antihistamines for longer duration.

Material and Methods

After getting ethical clearance from the ethical committee in the Heritage Institute of Medical College in November 2017, based on previous prevalence studies 138 consecutive patients of chronic urticaria were included in the study. After written consent, a detailed history and clinical examination were recorded for each patient.

Inclusion Criteria: Patients of chronic spontaneous urticaria were identified based on history, examination and routine laboratory investigations. History included use of drug for control of urticaria or drugs for other ailments known to suppress urticaria.

Routine investigations included complete blood count, stool examination, urine microscopy and

thyroid profile etc., to rule out possible causes of urticaria.

Exclusion Criteria: 1. Patients having acute urticaria (<6 weeks), physical urticarias including symptomatic dermographism (mechanical urticaria), solar urticaria, cold urticaria, pressure urticaria, cholinergic urticaria, contact urticaria syndromes, urticaria pigmentosa (mastocytosis), urticarial vasculitis. 2. Patients on immunosuppressive drugs during the last four weeks.

All patients with chronic spontaneous urticaria (CSU) were made to undergo antiTPO using chemiluminescence assay method.

ASST was performed on all patients diagnosed clinically as a case of CSU. For ASST 2ml blood was drawn by venepuncture and made to stand for 15 minutes to clot at room temperature then serum was separated by centrifugation at 500 rpm and was used immediately for ASST. Approximately 0.05 ml (2 units) in insulin syringe was drawn and injected intradermally on flexural aspect of the left forearm. Normal saline and histamine diphosphate was used as positive and negative control keeping a gap of 5 cm between the three test site. The test was considered positive when wheal size at ASST site was 1.5mm \geq than wheal at saline control site.

Data Analysis

All data was recorded and processed using SPSS version 12.0. While quantitative variables were expressed as mean (\pm SD), qualitative variables were expressed as frequencies and were compared using chi-square test. A p-value of <0.05 was considered significant. Mc Nemar test was performed and kappa calculated to see the agreement or disagreement between ASST and anti TPO.

Results and Discussion

Influence of demography on UAS score

As shown in Table 1 positive anti TPO was seen in more number of male patients than female patients but results were insignificant ($p > 0.05$). Not only this, even age did not show any

significant association with anti TPO in CSU patients. But anti TPO has shown a strong association with UAS7 score, hence with severity ($p < 0.05$).

Now, as in Table 3, UAS score is not associated with sex of the affected individual, we can conclude that female sex is not associated with severe form of CSU.

Has demography any effect on ASST & anti TPO ?

Parameters	Vikram kumar AG et al 2014.(11)	Najafipour M et al 2018.(12)	Present study
Age on ASST	Present		Absent
Sex on ASST	Present		Absent
Age on anti TPO		Absent	Absent
Sex on anti TPO		Absent	Absent

Has disease severity anything to do with ASST & anti TPO?

Since, chi-square and p-value (< 0.00001) shows significant association of ASST as well as anti TPO with UAS score (table 4&5), this suggests that, in our study both ASST & anti TPO have strong association with severity of CSU

What other studies have to say?

Comparison with our study

Study Parameter	Sabroe et al ¹⁰	Kulthanan et al ⁽¹³⁾	Georgeetal ⁽¹⁴⁾	Present study
ASST	Present	Absent	Present	Present
Autoantibodies (Serum IgE, Anti TPO, anti FCεR1 antibody)	Absent	Absent	Absent	Present

Anti TPO and ASST in CSU: associated or not ?
See table 5

Now, since both anti TPO and ASST are positive in greater number of patients of CSU, autoimmune basis of CSU is quite evident. Both McNemar test & kappa value denote that ASST is a better tool than anti TPO in excluding the cases

Table 1: Age Distribution of the Participants

	Mean	SD	Minimum	Maximum
Age (Years)	33.38	9.99	10	65

The mean age of the participants was 33.38 (± 9.99) years. The age ranged from 10 - 65 years.

of chronic autoimmune urticaria while the latter is a better option for screening cases of CAU.

Let's have a look at previous studies and compare them with ours.

In a study done by Letznoff et al in 1989 & Yokokuchi and his colleagues in 2003, significant association was reported between anti TPO antibodies and ASST positivity in case of chronic urticaria^(4,15). The findings of our study were inconsistent with these results, as in our study kappa value (-0.407) showed disagreement between antiTPO and ASST results. Even more, our results were unidentical to that of studies done by Bakos et al & O' Donnell et al who have reported significant association between anti TPO Ab and ASST positivity.^(16,17)

Though our findings were incomparable to the reports of Yadav et al and Jindal et al in 2017, who found no significant association between AMA & CAU.^(18,19), but were comparable to the study done by Aamir IS, Tauheed S, Majid S, Atif A who found that out of 47 patients diagnosed with chronic urticaria 42.65% had elevated anti thyroglobulin ab and 57.4% had raised ant microsomal ab levels.⁽²⁰⁾

Highlights

- ✚ UAS 7 score higher in individuals with positive anti TPO.
- ✚ UAS7 score higher in individuals with positive ASST.
- ✚ No sex predilection in CSU patients.
- ✚ All three of UAS score, anti TPO, ASST should be done in CSU patients.
- ✚ Anti TPO having higher sensitivity than ASST is a better screening tool for CSU patients.

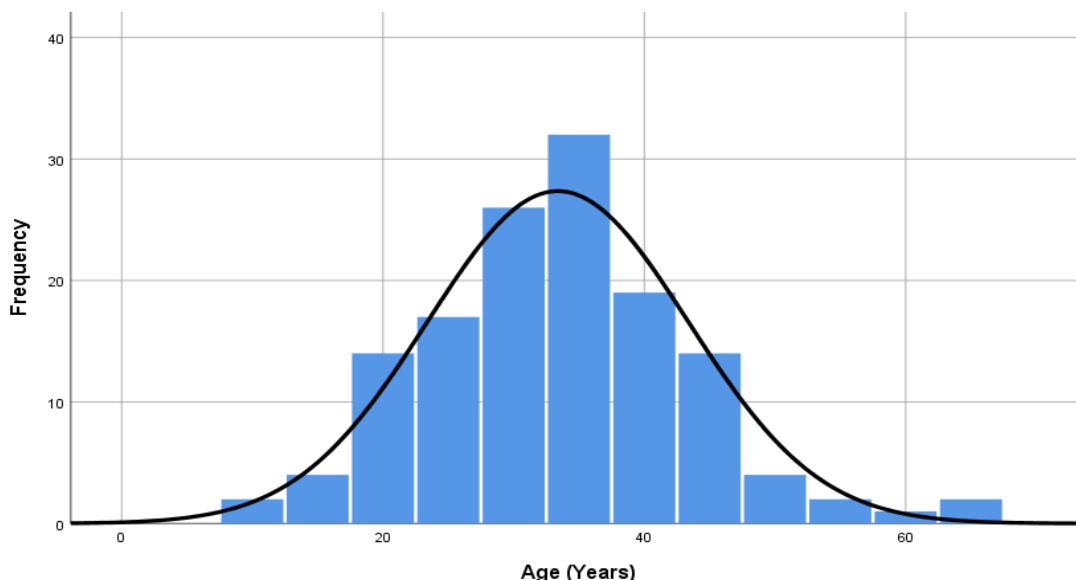


Table 2: Association of UAS Score with Gender

UAS Score	Gender				Total		Chi-Square Test	
	Male		Female					
	N	%	N	%	N	%	χ^2	P Value
Mild Activity	14	43.8%	56	53.3%	70	51.1%	1.350	0.509
Moderate Activity	11	34.4%	34	32.4%	45	32.8%		
Severe Activity	7	21.9%	15	14.3%	22	16.1%		
Total	32	100.0%	105	100.0%	137	100.0%		

43.8% patients in the Gender: Male group had UAS Score Mild Activity. 34.4% patients in the Gender: Male group had UAS Score Moderate Activity. 21.9% patients in the Gender: Male group had UAS Score Severe Activity. 53.3% patients in the Gender: Female group had UAS

Score Mild Activity. 32.4% patients in the Gender: Female group had UAS Score Moderate Activity. 14.3% patients in the Gender: Female group had UAS Score Severe Activity. There was no significant difference in the two groups in terms of UAS Score ($\chi^2 = 1.350, p = 0.509$).

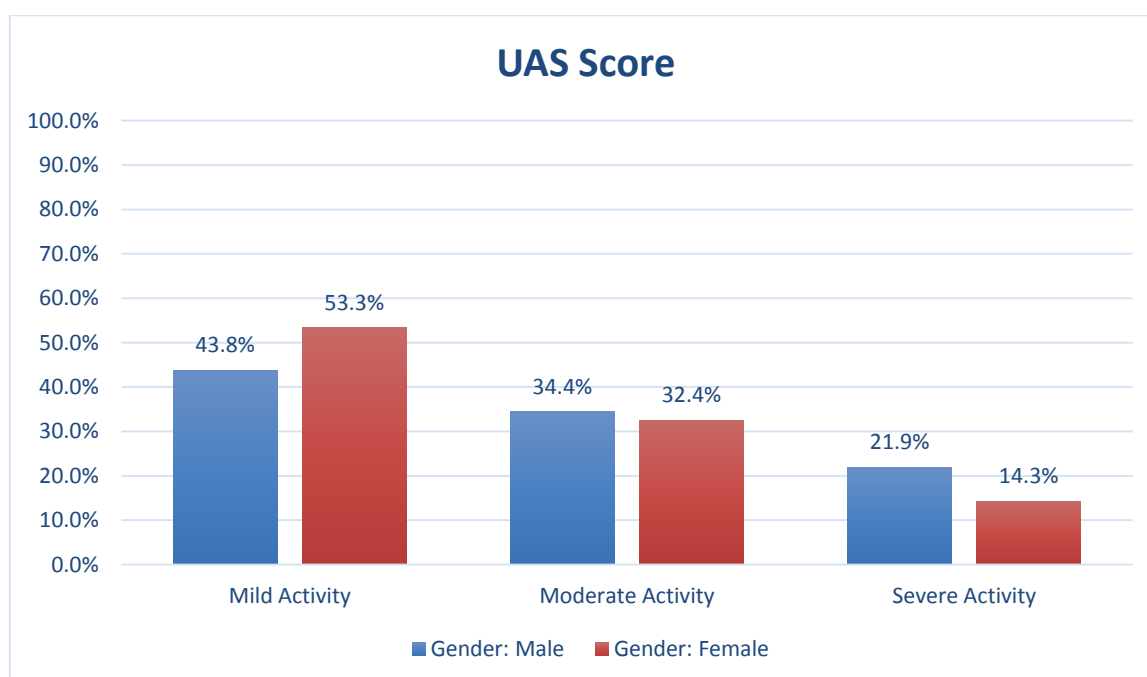


Table 3: Association of UAS Score with Anti-TPO

UAS Score	Anti-TPO				Total		Chi-Square Test	
	Positive		Negative					
	N	%	N	%	N	%	χ^2	P Value
Mild Activity	30	40.0%	40	64.5%	70	51.1%	11.003	0.004
Moderate Activity	27	36.0%	18	29.0%	45	32.8%		
Severe Activity	18	24.0%	4	6.5%	22	16.1%		
Total	75	100.0%	62	100.0%	137	100.0%		

40.0% patients in the Anti-TPO: Positive group had UAS Score Mild Activity. 36.0% patients in the Anti-TPO: Positive group had UAS Score Moderate Activity. 24.0% patients in the Anti-TPO: Positive group had UAS Score Severe Activity. 64.5% patients in the Anti-TPO: Negative group had UAS Score Mild Activity.

29.0% patients in the Anti-TPO: Negative group had UAS Score Moderate Activity. 6.5% patients in the Anti-TPO: Negative group had UAS Score Severe Activity. There was a significant difference in the two groups in terms of UAS Score ($\chi^2 = 11.003, p = 0.004$).

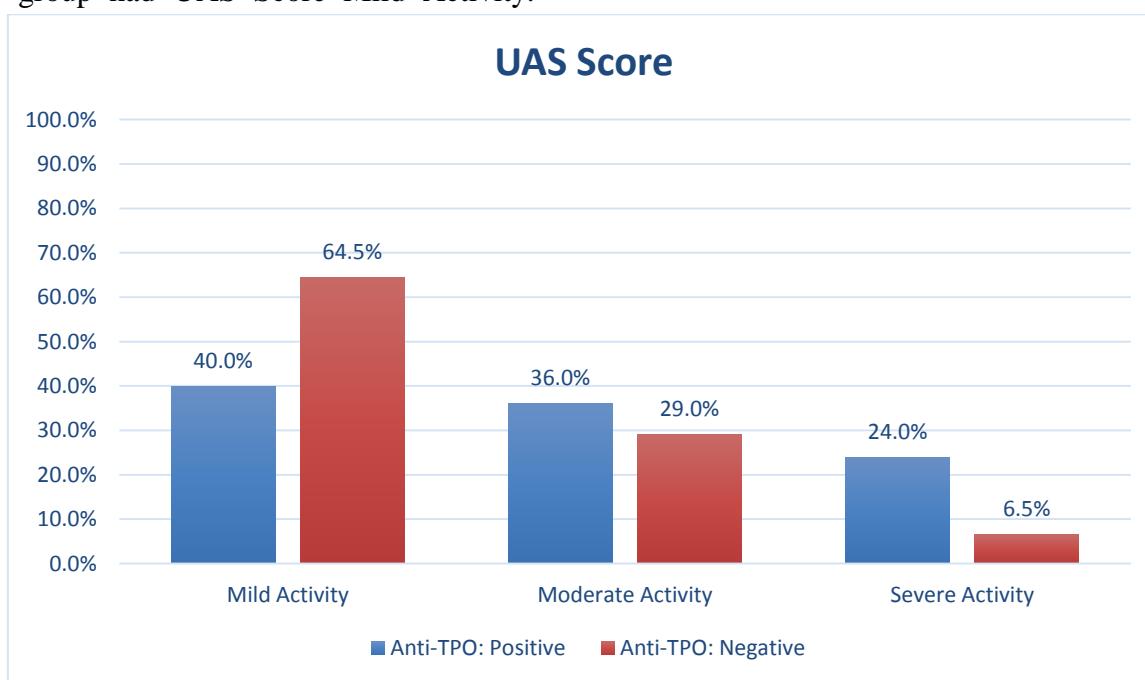


Table 4: Association of UAS Score with ASST

UAS Score	ASST				Total		Chi-Square Test	
	Positive		Negative					
	N	%	N	%	N	%	χ^2	P Value
Mild Activity	65	69.1%	5	11.6%	70	51.1%	42.965	<0.001
Moderate Activity	23	24.5%	22	51.2%	45	32.8%		
Severe Activity	6	6.4%	16	37.2%	22	16.1%		
Total	94	100.0%	43	100.0%	137	100.0%		

69.1% patients in the ASST: Positive group had UAS Score Mild Activity. 24.5% patients in the ASST: Positive group had UAS Score Moderate Activity. 6.4% patients in the ASST: Positive group had UAS Score Severe Activity. 11.6% patients in the ASST: Negative group had UAS

Score Mild Activity. 51.2% patients in the ASST: Negative group had UAS Score Moderate Activity. 37.2% patients in the ASST: Negative group had UAS Score Severe Activity. There was a significant difference in the two groups in terms of UAS Score ($\chi^2 = 42.965, p = <0.001$).

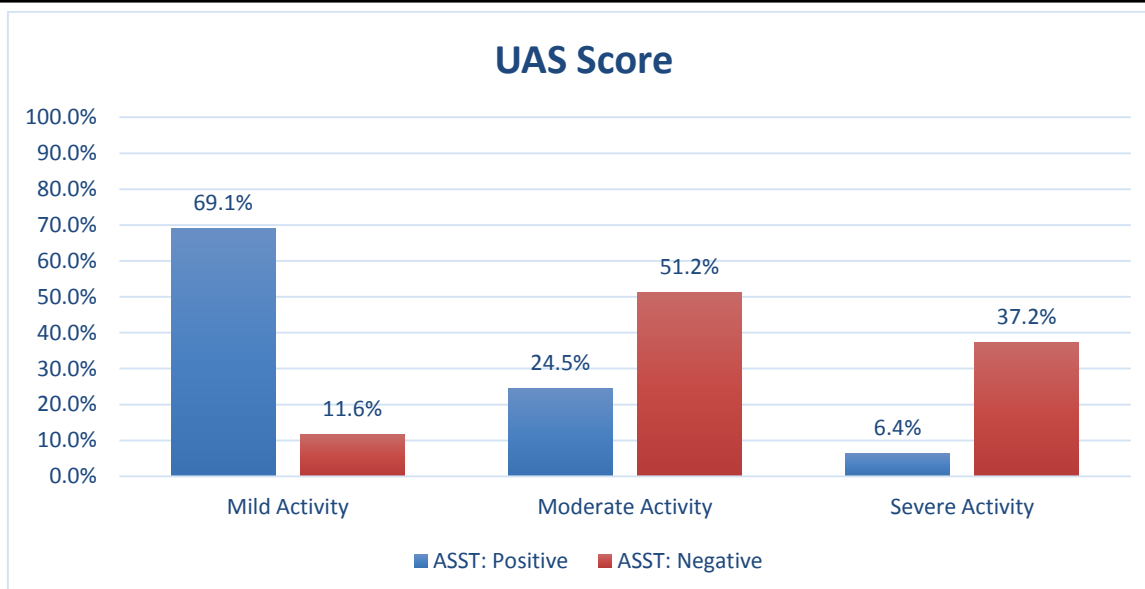
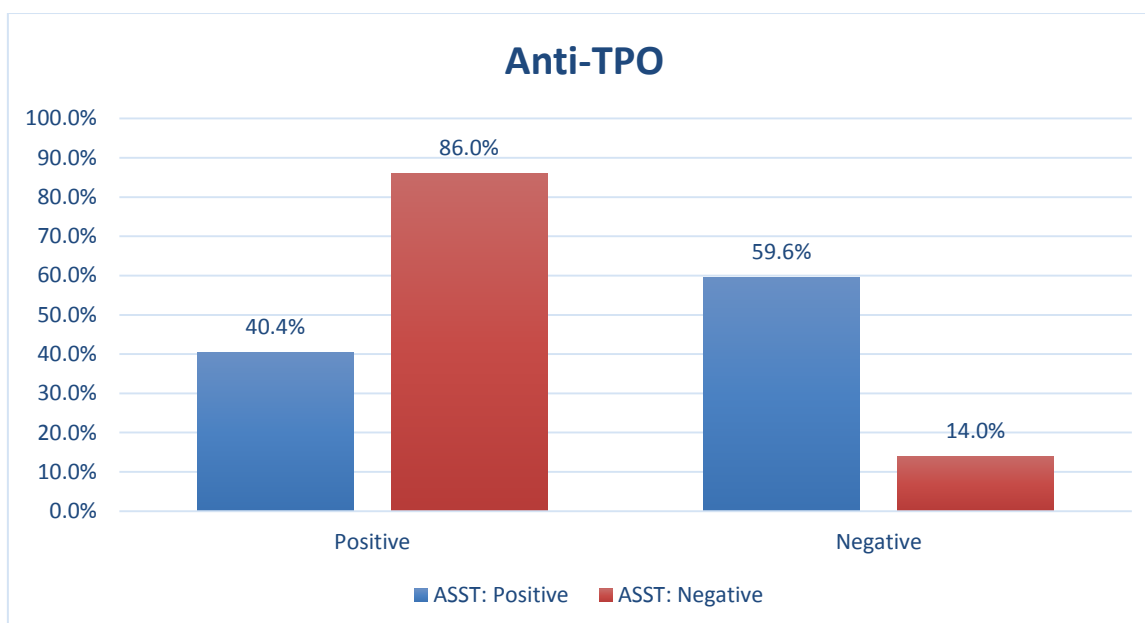


Table 5: Association of Anti-TPO with ASST

Anti-TPO	ASST				Total		McNemar's Test
	Positive		Negative		N	%	P Value
	N	%	N	%			
Positive	38	40.4%	37	86.0%	75	54.7%	
Negative	56	59.6%	6	14.0%	62	45.3%	
Total	94	100.0%	43	100.0%	137	100.0%	

40.4% patients in the ASST: Positive group had Anti-TPO Positive. 59.6% patients in the ASST: Positive group had Anti-TPO Negative. 86.0% patients in the ASST: Negative group had Anti-TPO Positive. 14.0% patients in the ASST: Negative group had Anti-TPO Negative. There was no significant disagreement between Anti-TPO and ASST (McNemar's Test: $p = 0.061$).

There was significant agreement between the two tests ($\text{kappa} = -0.407, p < 0.001$). The sensitivity and specificity of Anti-TPO as compared to ASST was 59.6% and 86% respectively, with negative TPO denoting a positive ASST,



Conclusion

We can conclude from our study that gender of patients has no significant association with severity of CAU but anti TPO has strong association with UAS score hence with severity of CAU. Even ASST positivity was found to be strongly associated with disease severity. Hence, inference drawn is that all CSU patients despite of their gender should be advised both ASST and Anti TPO.

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