Autologous serum skin test in chronic spontaneous urticaria: Evaluation of the relationship with disease activity and autoimmune antibodies

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ABSTRACT

Introduction: Chronic spontaneous urticaria (CSU) is a multifactorial, mast cell driven disorder characterized by wheals, angioedema, or both, lasting for more than six weeks. Autoimmunity, particularly Type IIb autoimmunity, involving IgG autoantibodies directed against either IgE or its high affinity receptor (FcεRI) on mast cells and basophils, plays a significant role in CSU pathogenesis. The Autologous Serum Skin Test (ASST) is a practical tool for detecting IgG autoantibodies and may be associated with the disease severity and the presences of autoimmune antibodies. Nonetheless, previous studies on ASST responses and the clinical features of patients with CSU have conflicting results.

Materials and Methods: This study aimed to establish the relationship between ASST positivity and disease activity, assessed by the Urticaria Activity Score 7 (UAS7) and to determine the associations with autoimmune antibodies including anti-thyroid peroxidase (anti-TPO), anti-thyroglobulin antibodies, and antinuclear antibodies (ANA). This cross- sectional study was conducted over a five months period, from January to May 2024, at the Department of Dermatology, in the tertiary hospital located in the capital city of Malaysia. Participants underwent ASST, laboratory evaluation for autoimmune antibodies, and assessment of disease activity using UAS7.

Results: In this study, 24 of the 59 patients were ASST positive, resulting in a prevalence rate of 41%. ASST positive patients demonstrated significantly higher disease activity, with a mean UAS7 score of 23.96 ± 10.55, compared to 13.51 ± 10.88 in ASST negative individuals (p = 0.001). A significant association was also found between ASST positivity and higher UAS7 severity categories (p = 0.011). Furthermore, a significant gender difference was observed with females more likely to exhibit ASST positivity (p = 0.016). Nevertheless, no significant associations were found between ASST results and presence of angioedema (p =1.0), atopy (p = 0.968), or autoimmune antibodies including ANA, anti-TPO, and anti-thyroglobulin antibodies (p > 0.05)

Conclusion: The significant association between ASST positivity and increased UAS7 scores heightened interplay between autoimmunity, disease severity, and clinical characteristics in CSU, particularly Type IIb autoimmunity subtype. Hence, ASST is a practical clinical tool for identifying autoimmune profile in CSU patients, and aids dermatologist in prognosis assessment and treatment strategies.

KEYWORDS:
Chronic spontaneous urticaria, autologous serum skin test, urticaria activity score 7, autoimmune antibodies

INTRODUCTION

Chronic spontaneous urticaria (CSU) is mast cell driven skin disorder characterized by recurrent wheals, angioedema, or both, persisting for more than six weeks.[1] The pathogenesis of CSU is multifactorial and complex. Several mechanisms have been contributing to the pathogenesis of CSU, including infections, food intolerance, coagulation cascade, genetic factors, and autoimmunity. Nowadays, increasing evidence suggest that autoimmunity plays a significant role in a subset of CSU patients. It is estimated that between 30 to 50% of CSU cases are autoimmune in nature, referred to as chronic autoimmune urticaria (CAU).[2-3] In these patients, the autoimmune response is primarily driven by functional autoantibodies that target mast cell and basophil receptors, leading to the mast cells degranulation and release of proinflammatory mediators responsible for the clinical manifestations of urticaria and angioedema.

According to the EAACI/GA²LEN/EuroGuiDerm/APAAACI guidelines published in 2021,[4] the pathogenesis of chronic urticaria can be categorized into different mechanisms, with Type I and Type IIb autoimmune pathways, with Type IIb being particularly relevant in chronic autoimmune urticaria.[4] Type I autoimmunity is characterized by the formation of IgE antibodies against allergens, which activate mast cells and basophils, commonly seen in allergic urticaria. In contrast, Type IIb autoimmunity involves IgG autoantibodies as the central players. These autoantibodies target IgE and FcεRIα receptors on mast cells and basophils. The binding of IgG autoantibodies to the receptors lead to mast cell degranulation and basophil activation, even in the absence of allergens, causing the release of histamine and other inflammatory mediators. The presence of these autoantibodies in Type IIb autoimmunity is a key feature of autoimmune CSU, and they can be detected using diagnostic tests such as the autologous serum skin test and the basophil histamine release assay.[3]

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Basophil histamine release assay (BHRA) remains the gold standard for detecting these autoantibodies in Type IIb autoimmunity. However, its complexity and limited availability necessitate simpler diagnostic alternatives. The autologous serum skin test (ASST) has emerged as a practical and widely accessible test to assess auto reactivity.[5-6]

Previous studies have demonstrated that patients with CSU and ASST positivity often experience greater disease activity, longer disease duration, diminished quality of life, and a higher frequency of concomitant angioedema.[6-8] However, some studies have failed to demonstrate significant correlation. This study aims to establish the association between ASST positivity and disease severity in patients with CSU, as well as its correlation with autoimmune antibodies in our study population. These findings may offer valuable insights for prognosis, guide treatment decisions, and support long term disease management in CSU patients.

The primary objective of this study is to establish the relationship between ASST positivity and disease activity, as measured by the UAS7, in patients diagnosed with CSU. UAS7 is a validated tool and widely use in both clinical practice and research by evaluating the number of wheals and the intensity of pruritus in patients with CSU.[4]

The secondary objective is to establish the association between ASST positivity and the presence of autoimmune biomarkers, including anti thyroid peroxidase (anti-TPO) antibodies, anti thyroglobulin antibodies, and antinuclear antibodies (ANA). These analyses aim to provide a deeper understanding of the immunological profile and disease severity within the study population

MATERIALS AND METHODS

This cross sectional study was conducted over a five months period, from January to May 2024, at the Skin Specialist Clinic Department of a tertiary hospital in a Malaysian state capital.

Ethical approval from the Medical Research and Ethics Committee (MREC) of the Ministry of Health (MOH) Malaysia, ID-23-02988-AEP (IIR), was obtained prior to the initiation of the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and the Malaysian Good Clinical Practice (GCP) guidelines

Eligible participants were adults aged 18 years or older who provided written informed consent. All participants had a confirmed diagnosis of chronic spontaneous urticaria (CSU), or CSU with concurrent inducible urticaria, with symptoms lasting for at least six weeks prior to enrolment. Participants were excluded if they met any of the following criteria: pregnancy or breastfeeding; needle phobia; severe, uncontrolled urticaria requiring continuous antihistamine use; chronic inducible urticaria without coexisting CSU; urticarial vasculitis; urticaria associated with autoinflammatory conditions such as Schnitzler syndrome or cryopyrin associated periodic syndromes; active malignancy; or active autoimmune disease on treatment. In addition, patients receiving high dose oral corticosteroids (more than 15 mg/day), cyclosporine, omalizumab or other immunosuppressive therapy such as methotrexate, azathioprine were also excluded.

Prior to undergoing the ASST, participants were instructed to discontinue antihistamines for at least 72 hours. They were also advised to avoid consuming any known foods that could trigger urticaria or allergic reactions.

The ASST was conducted following the standardized protocol recommended by the EAACI/GA²LEN task force consensus report to ensure accuracy and consistency.[7] Each participant was interviewed to collect demographic data, disease duration, triggering factors, and details about urticaria symptoms, including any episodes of angioedema or systemic involvement.

Venous blood samples were collected for laboratory investigations, including complete blood count, thyroid function tests, and autoimmune antibodies such as anti-thyroid peroxidase (anti-TPO), anti-thyroglobulin, and antinuclear antibodies (ANA). An additional blood sample was drawn into a plain tube to obtain serum for the ASST. This sample was allowed to clot at room temperature for 30 minutes and then centrifuged promptly. Fresh serum was used immediately to reduce the risk of contamination.

The ASST was performed on the volar side of the forearm that had been free from wheals for at least 24 hours. The skin was cleaned with normal saline, intradermal injections were administered using a 27G sterile syringe, spaced 3 cm apart. The test included three injections: 0.05 ml of normal saline as a negative control, 0.05 ml of the patient's serum, and a histamine solution as a positive control.

After 30 minutes, the injection sites were examined. The largest perpendicular diameters of the wheals were measured. A positive ASST result was defined as a serum-induced wheal that was at least 1.5 mm larger than the one from the normal saline control. The test was only considered valid if the histamine control produced a visible wheal.

Following the ASST, participants were asked to complete the Urticaria Activity Score 7 (UAS7) diary over the next seven days. Participants were asked to avoid antihistamines during this period.

Statistical Analysis

Data were cleaned and analyzed using SPSS version 26.0. The distribution of continuous variables was assessed through measures of skewness and kurtosis, as well as visual inspection of histograms. Continuous variables were presented as mean ± standard deviation when normally distributed, and as median when the data were not normally distributed. Categorical variables were presented as frequency and percentage.

The association between the Urticaria Activity Score 7 and the autologous serum skin test, disease duration and eosinophilia were analysed using independent sample t-tests, Kruskal-Wallis tests, Fisher's exact tests, and correlation

analyses. Additionally, the relationship between ASST results and the presence of autoantibodies was assessed using Fisher's exact test. All tests were two-sided, with statistical significance set at $p < 0.05$.

Ethics Approval

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RESULTS

The study included a total of 59 participants, with a mean age of 47 years. The majority of the sample were female, constituting 76.3% of the study population, while males accounted for 23.7%. The ethnic composition was diverse, with Malay (49.2%), Chinese (35.6%), Indian (13.6%), and Filippino (1.7%) represented. The reported comorbidities encompassed metabolic disorders (45.7%), cardiovascular conditions (6.7%), hypothyroidism (6.7%), and connective tissue disorders (6.7%) and neurological disease (1.7%). Notably, no participants had a history of vitiligo, type 1 diabetes, or inflammatory bowel disease (Table I).

The study found that 40.7% of the participants had a personal history of atopic conditions. Additionally, 30.5% of the participants reported a family history of atopy, 23.7% had a family history of chronic urticaria, and 22% had a family history of autoimmune diseases (Table I).

The clinical characteristics of the patients are summarized in Table II. The median duration of disease activity was 12 months. The distribution of urticarial lesions varied among patients, with the lower limbs being the most frequently affected site, observed in 94.9% of cases. This was followed by involvement of the upper limbs in 93.2% of patients, the trunk in 89.8%, and the face in 52.5%. A significant proportion of patients experienced angioedema, 35 patients (59.3%) reported a history of at least one episode of angioedema (Table II).

Regarding laboratory findings, elevated eosinophil counts were detected in 6 patients (10.2%), while abnormal thyroid function tests were observed in 2 patients (3.4%). The presence of autoantibodies was also noted, with anti-thyroid peroxidase (anti-TPO) antibodies in 16.9%, and anti-thyroglobulin antibodies in 22.0% of patients and antinuclear antibodies (ANA) detected in 16.9% of patients (Table II).

In this study, 24 patients (40.7%) exhibited a positive ASST result, while the remaining 59.0% had a negative ASST result (Table II). ASST was performed to assess the presence of autoreactivity in patients with chronic urticaria. ASST is a widely used diagnostic tool that evaluates the presence of circulating histamine-releasing autoantibodies, which contribute to the pathophysiology of chronic spontaneous urticaria (CSU).

In this study, the mean UAS7 score was 17.76 (standard deviation [SD]: 11.84), reflecting a broad spectrum of disease severity among participants. 22.0% of participants were classified as having well-controlled disease (UAS7: 0–6), mild disease activity (UAS7: 7–15) was observed in 25.4% of patients, while 30.5% exhibited moderate disease severity (UAS7: 16–27). Notably, 22.0% of participants experienced severe urticaria (UAS7: 28–42), characterized by frequent and intense symptoms significantly impacting daily life (Table II).

The study found a statistically significant difference in the autologous serum skin test results between genders. The data showed that 55.6% of the female participants had a positive ASST, compared to only 14.3% of the male participants. This difference was found to be statistically significant, with a p-value of 0.016. This suggests that female participants with chronic spontaneous urticaria were more likely to exhibit a positive ASST response compared to male participants (Table III).

The results of our analysis did not indicate a statistically significant relationship between the occurrence of angioedema and the outcome of the autologous serum skin test. Among participants with history of angioedema, 51.4% exhibited a positive ASST result, while 50% of those without angiodema also showed a positive ASST. This finding suggests that the presence or absence of angioedema did not significantly influence the ASST results (Table III).

The analysis revealed that among participants with a positive autologous serum skin test, 45.8% had a personal history of atopic diseases. In contrast, a higher proportion of 54.2% of participants with negative ASST had a personal history of atopy. However, the p-value of 0.968 indicates a lack of statistical significance in the association between atopy and ASST positivity. This suggests that the ASST results may be more reflective of the autoimmune mechanisms underlying chronic spontaneous urticaria, rather than being primarily driven by IgE mediated mast cell degranulation (Table III).

Patients who tested positive for the ASST exhibited significantly higher USA7 scores compared to those with negative ASST results. The mean USA7 score for patients with a negative ASST result was 13.51 ± 10.88, while for those with a positive ASST, the mean score was 23.96 ± 10.55 ($p = 0.001$). This indicates that patients with positive ASST results had a notably higher disease severity, as reflected by the USA7 scores, which assess the severity of skin involvement (Table IV).

In addition, a higher proportion of patients with a negative ASST test were found to have well controlled or mild disease severity. In contrast, patients with positive ASST results tended to show higher proportions of moderate to severe disease severity. Therefore, a statistically significant association was observed between the USA7 score categories and ASST results ($p = 0.011$) (Table IV).

In this study, the results of the positive ASST was compared to the auto antibody markers (Anti Nuclear Antibody (ANA), Anti Thyroid Peroxidase (Anti-TPO) and Anti-thyroglobulin) using chi square test. It was found that there was no

Table I: Demographics of study population

Characteristic	Findings	N (%)
Age in years, mean ± SD	47.1 ± 15.1	
Gender	Female	45 (76.3)
	Male	14 (23.7)
Ethnicity	Malay	29 (49.1)
	Chinese	21 (35.6)
	Indian	8 (13.6)
	Filippino	1 (1.7)
Comorbidities	Metabolic disease	27 (45.7)
	Heart disease	4 (6.7)
	Thyroid disease	4 (6.7)
	Connective tissue disease	4 (6.7)
	Neurological disease	1 (1.7)
	Vitiligo	0 (0)
	Type 1 diabetes mellitus	0 (0)
	Inflammatory bowel disease	0 (0)
Personal history of atopy	Yes	24 (40.7)
	No	35 (59.3)
Family history	Atopy	18 (30.5)
	Chronic urticaria	14 (23.7)
	Autoimmune disease	13 (22.0)

Table II: Clinical characteristics of study population

Characteristics	Findings	N (%)
Duration of disease in months, Median	2 to 120	12 months
Distribution of urticaria	Lower limb	56 (94.9)
	Upper limb	55 (93.2)
	Trunk	53 (89.8)
	Face	31 (52.5)
History of angioedema	Yes	35 (59.3)
	No	24 (40.7)
ASST	Postive	24 (40.7)
	Negative	35 (59.3)
UAS 7 Mean score ± SD	17.76 ± 11.84	
USA 7 in severity category	Well controlled (1-6)	13 (22.0)
	Mild (7-15)	15 (25.5)
	Moderate (16-27)	18 (30.5)
	Severe (28-42)	13 (22.0)
Eo0sinophil count	Normal (> 0.5 x10^9/L)	53 (89.8)
	Elevated (< 0.5 x10^9/L)	6 (10.2)
Thyroid function test	Normal	57 (96.6)
	Abnormal	2 (3.4)
Anti thyroid peroxidase	Normal	49 (83.1)
	Elevated	10 (16.9)
Anti thyroglobulin	Normal	47 (78.0)
	Elevated	13 (22.0)
Antinuclear antibody	Negative	49 (83.1)
	Positive	10 (16.9)

Table III: Association of autologous serum skin test and gender, angioedema and personal atopy disease

Characteristics	ASST positive N (%)	ASST negative N (%)	p-value
Gender			0.016
• Female	25 (55.6%)	20 (44.4%)	
• Male	2 (14.3%)	12 (85.7%)	
Angioedema			1
• Yes	18 (51.4%)	17 (48.6%)	
• No	12 (50%)	12 (50%) 1	
Atopy disease			0.968
• Yes	11 (45.8%)	13 (54.2%)	
• No	16 (45.7%)	19 (54.3%)	

Table IV: Association of autologous serum skin test with disease activity and autoimmune autoantibodies

Disease severity	ASST positive N (%)	ASST negative N (%)	p-value
UAS 7 score, mean ± SD	23.96 ± 10.55	13.51 ± 10.88	0.001
UAS 7 in severity category			
• Well controlled	1 (4.2)	12 (43.3)	
• Mild	5 (20.8)	10 (28.6)	0.011
• Moderate	9 (37.5)	9 (24.7)	
• Severe	9 (37.5)	4 (11.4)	
ANA			
• Non reactive	21(87.5)	28 (80.0)	0.506
• Reactive	3 (12.5)	7 (20.0)	
Anti TPO			
• Normal	20 (83.3)	29 (82.9)	> 0.950
• Elevate	4(16.7)	6 (17.1)	
Antithyroglobulin			
• Normal	19 (79.2)	27 (77.1)	>0.950
• Elevate	5 (20.8)	8 (22.9)	

Table V: Association of elevated eosinophils, presence of autoantibodies with disease activity based on UAS 7

Blood parameters	Well controlled	Mild	Moderate	Severe	p-value
Eosinophil count					0.126
• Normal	11(84.6)	14 (93.3)	18 (100.0)	10 (76.9)	
• Elevate	2(15.4)	1 (6.7)	0 (0.0)	3 (23.1)	
ANA					0.195
• Non reactive	9 (69.2)	12 (80.0)	15 (83.3)	13 (100.0)	
• Reactive	4 (30.8)	3 (20.0)	3 (16.7)	0 (0.0)	
Anti TPO					0.313
• Normal	9 (69.2)	12 (80.0)	17 (94.4)	11 (84.6)	
• Elevate	4 (30.8)	3 (20.0)	1(5.6)	2 (15.4)	
Antithyroglobulin					0.356
• Normal	9 (69.2)	10 (66.7)	16 (88.9)	11 (84.6)	
• Elevate	4 (30.8)	5 (33.3)	2 (11.1)	2 (15.4)	

statistical significant difference with the ANA (p=0.51), Anti-TPO (p=0.99) and Anti-thyroglobulin (p=0.99)(Table IV).

In this study, we aimed to investigate the relationship between elevated eosinophil levels, the presence of autoantibodies, and disease severity, as assessed by the UAS7 score. Despite our analysis using Fisher Exact test, no significant correlations were observed between these factors and the severity of the disease. All results yielded a p-value greater than 0.05, indicating the lack of a statistical significant association. (Table V).

The analysis revealed that the mean duration of the disease was shorter in the severe group compared to the other groups. However, this difference was not statistically significant, with a p-value of 0.147.

DISCUSSION

The current study aims to provide better insight into the clinical characteristics of CSU, the relationship between the outcomes of ASST with the clinical presentation, disease activity and the presence of autoimmune auto-antibodies.

Our study demonstrated a statistically significant gender different in ASST positivity among CSU patients, with females representing 76.3% of ASST positive cases (p = 0.016). This observation is consistent with earlier studies reporting a higher prevalence of CSU in women, which may be influenced by hormonal factors.[8-9] Women have higher levels of oestrogen and progesterone, whereas men exhibit increased levels of dehydroepiandrosterone sulphate (DHEAS), a hormone with anti inflammatory and immuno-modulatory properties. Serum concentrations of DHEAS in CSU patients are significantly lower than those in healthy subjects and are associated with positive responses to ASST.[10] These hormonal differences are believed to influence immune responses and may contribute to the greater autoimmune activity seen in female CSU patients, potentially explaining their higher ASST positivity.

Angioedema is the clinical manifestation of urticaria, located within the subcutis. Although angioedema is commonly observed in CSU, occurring in 30-50% of cases.[3] The relationship between angioedema and the outcomes of the autologous serum skin test remains unclear. Some studies have suggested that CSU patients with angioedema may experience a more prolonged and severe disease course.[8-9] This has been attributed to the potential role of functional autoantibodies, particularly those targeting IgE and FcεRI, in triggering stronger and more prolonged mast cell activation, which could increase the risk of severe urticaria and angioedema. Type IIb autoimmunity characterized by these autoantibodies has been associated with severe CSU and recurrent, prolonged angioedema, especially in individuals with positive ASST results.[3,11-12] However, the current study did not find a statistically significant association between the

presence of angioedema and ASST positivity. This lack of significance may be attributed to sample size limitations or individual variability in immune responses.

Previous studies have shown that patients with chronic urticaria exhibit a higher prevalence of atopic conditions, such as allergic rhinitis, asthma, and atopic dermatitis, compared to control groups.[13-14] Our study corroborates these findings, with 40.6% of participants reporting a personal history of atopic disorders and 30.5% having a family history of atopy. However, further analysis did not reveal a significant association between a personal history of atopy and positive results on the autologous serum skin test. This is due to difference autoimmune mechanism in between Type 1 and Type IIb autoimmunity. Type I CSU is linked to IgE mediated mechanisms, with patients often exhibiting higher total IgE levels and more pronounced atopic features. In contrast, Type IIb CSU is associated with the presence of autoantibodies, such as IgG or IgM targeting the IgE receptor and FcεRI, and is frequently characterized by low total IgE levels and a positive autologous serum skin test.[15] Therefore, in our study, the positive ASST findings suggest the presence of Type IIb autoimmunity in CSU, which is driven by autoantibodies rather than atopic predisposition.

The participants in our study were well distributed across different disease severity levels based on the Urticaria Activity Score 7 (UAS7), a validated tool used to assess disease activity in CSU. The UAS7 score assesses the frequency and intensity of wheals and pruritus over severe days. The majority of our participants with positive ASST fell into the moderate and severity category, with ($p = 0.011$). According to a study by Alyasin et all, patients with a positive ASST had more severe CSU, characterized by larger wheal size, longer disease duration, and higher attack frequency.[16] Our finding align with these observations, indicating that individuals with positive ASST results demonstrated significantly higher mean UAS7, with a statistically significant p value of 0.001. This suggests that these individuals exhibited more severe disease symptoms compared to those with negative ASST results. The presence of autoantibodies, such as IgG and IgM directed against the IgE receptor and FcεRI, may contribute to the increased severity and persistence of symptoms in chronic spontaneous urticaria patients.[17-19]

In addition, ASST is an effective clinical screening tool for detecting functional circulating autoantibodies in patients with CSU. It has demonstrated approximately 70% sensitivity and 80% specificity in identifying the autoimmune subset of CSU.[6] This screening test has a negative predictive value of approximately 82.5±14%, indicating that in CSU patients with a negative ASST response, there is a high likelihood that no functional circulating autoantibodies are present in their serum.[9,20-22]

Chronic spontaneous urticaria is strongly associated with various autoimmune conditions, including autoimmune thyroiditis, celiac disease, rheumatoid arthritis, Graves' disease, vitiligo and type 1 diabetes.[7,23] Among these, thyroid disease is the most frequently reported autoimmune condition in CSU patients.[24-25] Individuals with thyroid dysfunction often experience a more severe and prolonged course of CSU compared to those without thyroid abnormalities.[12,26] Type IIb autoimmunity, characterized by the presence of functional autoantibodies such as IgG anti thyroid peroxidase, is increasingly recognized as a key driver of autoimmune CSU.[3] Even clinically euthyroid CSU patients may have persistent anti-thyroid antibodies, indicating an underlying autoimmune mechanism.

A study by Ismail et al in Malaysia, found that 23% of chronic urticaria patients had anti TPO antibodies compared to 8% in the control group, reinforcing the higher prevalence of thyroid autoimmunity in CSU.[10] The activation of the complement system by thyroid autoantibodies may exacerbate urticaria, leading to increased inflammation and prolonged disease activity. This suggests that the presence of these autoantibodies, as detected by ASST, could contribute to the severity and persistence of CSU symptoms. While our study did not find a statistically significant association between the presence of autoantibodies, such as ANA, anti-TPO, and anti-thyroglobulin, and the results of the autologous serum skin test, this discrepancy may be attributed to the relatively small sample size and heterogeneity of the study population. Further large scale studies are needed to assess the complex relationships between autoantibodies, disease activity, and clinical features in patients with CSU.

CONCLUSION

This study showed the interplay between autoimmunity, disease severity, and clinical characteristics in chronic spontaneous urticaria. Our findings support the association between positive ASST and increased CSU severity, with ASST positive individuals exhibiting significantly higher UAS7 score. Furthermore, the observed gender disparity suggests a potential hormonal influence on ASST reactivity, leading to a higher prevalence of positive ASST results among female participants. However, no significant associations were observed between ASST positivity and atopy, angioedema, or thyroid related autoimmune antibodies. Given its simplicity, low cost, and wide availability, the ASST remains a valuable tool for evaluating disease severity and supporting clinical decision making in the management of CSU.

CONFLICT OF INTEREST

The authors declare no conflicts of interest regarding the research, no relevant financial or non-financial interest to disclose.

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