

A Comparison of Autologous Serum, Plasma, and Whole Blood for Intradermal Autoreactivity Testing in Patients with Chronic Spontaneous Urticarial: A Cross-Sectional Study

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Abstract

Background: Autologous serum (ASST) and plasma (APST) skin testing confirm autoreactivity in chronic spontaneous urticaria (CSU). Whole blood autohemotherapy has been used. Plasma and even whole blood may be used instead of serum with relatively quicker preparation and cheaper method especially using the latter in centers with limited resources. **Purpose:** The purpose of the study is to determine if similar intradermal skin reactions can be observed when using either serum, plasma, or whole blood in autologous skin tests and to determine factors associated with positive tests and wheal diameter. **Methods:** We performed a cross-sectional study of chronic urticaria patients in a dermatology clinic. Tests were performed according to EAACI/GA2 LEN Task Force recommendations. Urticaria Activity Score over 7 days (UAS7) was assessed. Statistical analyses included Chi-square, Mann-Whitney U, Spearman's, and Wilcoxon rank tests. **Results:** Twenty-six (77%) females and 8 (24%) males mean age 34 (26–42) years participated. ASST, APST and autologous whole blood for skin testing (AWBST) positivity rates were 24%, 29% and 27%, respectively ($P = 0.86$). 13 (38%) had at least 1 positive test; all tests were negative in 21 (62%). All tests were positive in 7 (21%), 3 (23%) were positive APST alone, 2 (15%) AWBST, 1 (8%) ASST. Pretest UAS7 was higher with those with test positive ($P = 0.04$). Test results were unaffected by age, gender, disease duration, atopy, anti-nuclear antibody, and thyroid status. Wheal diameter correlated with thyroid-stimulating hormone ($P = 0.04$). **Conclusion:** Autoreactivity rates were similar with ASST, APST, and AWBST. Positive tests were associated with severe CSU. Autologous whole blood may be a simpler and less costly alternative to plasma and serum for autoreactivity skin testing in patients with chronic urticaria.

Keywords: Chronic spontaneous urticaria, plasma, serum, skin test, urticaria

INTRODUCTION

Chronic spontaneous urticaria (CSU) is defined as the development of wheals, angioedema, or both for a duration of 6 weeks or more with no obvious triggers.^[1] The point prevalence of CSU is 0.8% at our center^[2] with worldwide prevalence between 0.5% and 1%.^[3] Peak incidence occurs between the age 20 and 40 years old and typically last between 1 to 5 years.^[3]

CSU is largely a mast cell-driven process.^[1] Histamine and other mediators, such as platelet-activating factor and cytokines, are released from mast cells.^[1] Sensory neural activation, vasodilatation, plasma extravasation, and recruitment of other cells ensues.^[1] However, mast cell-activating signals in

urticaria are ill-defined and likely to be heterogeneous and diverse.^[1]

Autologous serum skin test (ASST) is an *in vivo* test for autoreactivity.^[4] Autoreactivity is reflected by the development of wheals after injecting autologous serum intradermally. Autoreactivity does not translate into

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autoimmune urticaria but may be an indication of mast cell activating autoantibodies.^[4] Refractory CSU occurs in those with severe disease, concurrent angioedema or inducible urticaria, and positive ASST.^[3] ASST positivity was associated with disease refractory to antihistamine.^[5] Hence, we are able to identify those requiring second-line agents like omalizumab or ciclosporin much earlier and introducing these rather than changing different antihistamines or continuing for longer duration.

Autologous plasma skin test (APST) compared against ASST showed 86% APST positivity versus 56% for ASST.^[6] APST may have better specificity as plasma contains more complement and coagulation factors.^[3,4] Thrombin is able to trigger mast cell degranulation and activate protease-activated receptor 1 (PAR-1) on mast cells.^[7] Response to thrombin is equipotent with FcεRI-mediated activation in some mast cell populations.^[8] Protease-activated receptor-2 (PAR-2) activation is further enabled by factor VIIa, factor Xa, and tissue factor complex.^[9] These are the basis for successful utilization of anticoagulants such as warfarin and low-molecular-weight heparin in the treatment of refractory CSU, especially in patients with elevated D-dimer.^[10,11]

The use of autologous whole blood for skin testing (AWBST) is not well characterized. Circulating histamine-releasing factors may be present within patients' own blood. Basophil releasing assays detect functional anti-FcεRI or anti-immunoglobulin E (IgE) autoantibodies in 30%–50% of CSU patients.^[12] Autohemotherapy protocols to desensitize against these triggering factors were devised based on this concept.^[5,13,14] AWBST could be useful in developing countries because it is a less costly option compared to preparing serum for ASST. The aim of this study was to compare the positivity rate of AWBST, APST, and ASST in patients with CSU, to determine factors associated with tests' positivity, and to determine the relationship between wheal diameter with disease severity and other clinical factors.

METHODS

A cross-sectional study was conducted at the Dermatology Clinic, University Kebangsaan Malaysia Medical Centre. CSU patients aged between 18 and 65 years old were included. Exclusion criteria included pregnant and lactating women and those on anticoagulation or systemic immunosuppressive therapy. The study protocol was approved by the Research Ethics Committee, University Kebangsaan Malaysia, Kuala Lumpur, Malaysia Project code FF-2018-347. Informed consent of all participating subjects was obtained.

Sample size calculation used point prevalence formula adjusted for finite population: $n = (Z^2 P(1-P))/d^2$,^[15] Z value for a level of confidence 95% equals to 1.96. P was expected prevalence ($P = 0.008$) and d is the precision ($d = 5\%$ or 0.05). We obtained 35 samples over a 1-year period using point prevalence of current population for all 3 different assessments of skin tests.

Demographic and clinical characteristics were obtained by a face-to-face interview and physical examination. Urticaria Activity Score over 7 days (UAS7) and Dermatology Life Quality Index (DLQI) were assessed. Laboratory investigations included full blood count, thyroid function test, and anti-nuclear antibody (ANA). Subjects were informed to withhold antihistamines for at least 3 days before skin testing and were assumed to comply with our instruction.

Serum was prepared according to the EAACI/GA2 LEN Task Force recommendation.^[4] Four ml of venous blood was collected in a 7 ml Becton Dickinson (BD[®]) vacutainer with no additive, left at room temperature for 30 min. Centrifugation was performed at 1.9×1000 revolutions per minute (RPM) for 10 min using Medifuge[®] Thermo Scientific. Plasma was prepared by drawing 4 ml of venous blood into buffered sodium citrate BD[®] vacutainer, allowed to clot at room temperature for 15 min, and centrifuged for 3 min at 3.1×1000 RPM.^[16] Venous blood was drawn and used immediately as autologous whole blood component, following the preparation for AWB autohemotherapy.^[5] Skin tests were performed by a single investigator according to the EAACI/GA2 LEN Task Force recommendation.^[4] A volume of 0.05 ml of each blood component was aspirated into a 1 ml sterile BD[®] syringe with 26G \times 12 mm needle (SJ[®] Needle) without dead space. The syringes were covered with opaque sticker to blind both the patient and the investigator. Intradermal injections were made aiming to raise a palpable bleb of fluid at the volar aspect of the forearm. A five cm gap was left between each of the injections. The sequence of skin tests for each patient was randomized. A positive histamine control was performed by skin prick (10 mg/ml), whereas intradermal injection of saline served as negative control.

Results of skin testing were evaluated by a dedicated investigator at 15 and 30 min. Mean wheal diameter was documented using two longest perpendicular diameter (in mm) measured with a clean transparent ruler pressed lightly onto the skin surface. Mean wheal diameter of skin test minus mean wheal diameter of negative control equal or more than 1.5 mm at 30 min is considered positive.^[4]

Analyses were performed using IBM[®] SPSS[®] Statistics version 23. A $P < 0.05$ was considered statistically significant. Descriptive statistics were used to summarize demographic information and test prevalences. Chi-square test compared differences between two categorical data, Mann–Whitney U-test compared group differences of continuous data, whereas Spearman's test was used to analyze correlations between continuous data. Wilcoxon rank test was used to see improvement over time and logistic regression was used to analyze impact of covariates upon different types of skin tests.

RESULTS

Thirty-four patients were recruited into the study, 26 (77%) were females and 8 (24%) were males with median age 34 years old [Table 1]. Median duration of CSU was 24 (40.3)

months. There was associated angioedema in 14 (41%) and anaphylaxis in 2 (6%) of patients. Median UAS7 was 9 (13), median DLQI was 6.5 (9). Three (9%) of patients had atopic dermatitis (AD), 6 (8%) allergic rhinitis (AR), and 7 (21%) bronchial asthma (BA). There were 6 (18%) patients with family history of AD, 3 (9%) AR, and 14 (41%) BA. Majority of subjects were on levocetirizine 18 (53%), followed by loratadine 14 (41%) and bilaxtine 2 (6%).

Table 1: Demography, clinical characteristic and laboratory parameters of study population (n=34)

Parameters	n=34, n (%) or median (IQR)
Age (years)	33.5 (16)
Gender	
Female	26 (77)
Male	8 (24)
Clinical characteristics	n (%) or median (IQR)
Duration of CSU (months)	24 (40.3)
Associated angioedema	14 (41)
Anaphylaxis	2 (6)
CSU severity	
UAS7-pre, n=34	9 (13)
UAS7-post, n=25	7 (15.5)
DLQI-pre, n=34	6.5 (9.0)
DLQI-post, n=25	3.5 (8.8)
Atopy history	
AD	3 (9)
AR	6 (18)
BA	7 (21)
Family atopy	
AD	6 (18)
AR	3 (9)
BA	14 (41)
Laboratory parameters (units)	Median (IQR)
Eos ($\times 10^9$)	0.2 (0.1)
Plat ($\times 10^9$)	302 (76)
WBC ($\times 10^9$)	7.5 (2.3)
Hb (g/dL)	13.8 (2.0)
C3 (mg/dL)	106 (40.3)
C4 (mg/dL)	25.3 (10.4)
Thyroid stimulating hormone (m IU/L), n=29	1.15 (1.2)
Normal	27 (93.1)
Abnormal (low)	2 (6.9)
Free T4 (p IU/L), n=29	12.8 (1.9)
Normal	27 (93.1)
Abnormal (high)	2 (6.9)
Anti-nuclear antibody positive	3 (8.8)
CSU treatment	
Levocetirizine	18 (53)
Loratadine	14 (41)
Bilaxtine	2 (6)

CSU: Chronic spontaneous urticarial, AD: Atopic dermatitis, AR: Allergic rhinitis, BA: Bronchial asthma, UAS7: Urticaria activity score over 7 days, DLQI: Dermatology Life Quality Index, TSH: Thyroid-stimulating hormone, WBC: White blood cell, Hb: Hemoglobin, Eos: Eosinophil, Plat: Platelet, IQR: Interquartile range

Laboratory parameters performed before skin tests including eosinophils, hemoglobin, and complement levels were within normal ranges [Table 1]. There were 2 (6%) patients with abnormal thyroid function tests, both were hyperthyroid and 3 (9%) patients had positive ANA.

All patients demonstrated a reaction to all the tests ($P < 0.001$) with mean wheal diameter of 3.4 ± 1.6 mm at 30 min. However, when wheal diameter of skin test minus negative control was ≥ 1.5 mm used to define a positive result; ASST, APST, and AWBST positivity rates were 8 (24%), 10 (29%), and 9 (27%), respectively. There was no statistically significant difference between ASST, APST, and AWBST positivity rates [$P = 0.86$, Figure 1]. Thirteen patients (38%) showed at least 1 positive test, while 21 (62%) were negative to all tests. All tests were positive in 7 (21%) subjects, 3 (23%) in APST alone, 2 (15%) AWBST, and 1 (8%) ASST. UAS7 were higher in patients with positive test (17 [15%]) compared to those who tested negative (7 [13.5%]) [Table 2].

Autologous skin test positivity was not affected by age, gender, disease duration, history of atopy, family history of atopy, anaphylaxis history, associated angioedema, ANA positivity, and thyroid status. There were no significant differences between serum, plasma, or serum when analyzed against these characteristics [Table 3]. Mean wheal diameters were positively correlated to TSH level [$r_s = 0.66$, $P = 0.04$, Table 4].

DISCUSSION

ASST is one of the diagnostic tests available for CSU.^[1,4] APST may have better positive and negative predictive values than ASST.^[16] In previous studies, between 39.5% and 70% of patients with negative ASST tested positive with APST^[6,17,18] while all patients with negative APST did not develop a reaction with ASST.^[17] All patients who were ASST positive were also APST positive but an additional 22% were only

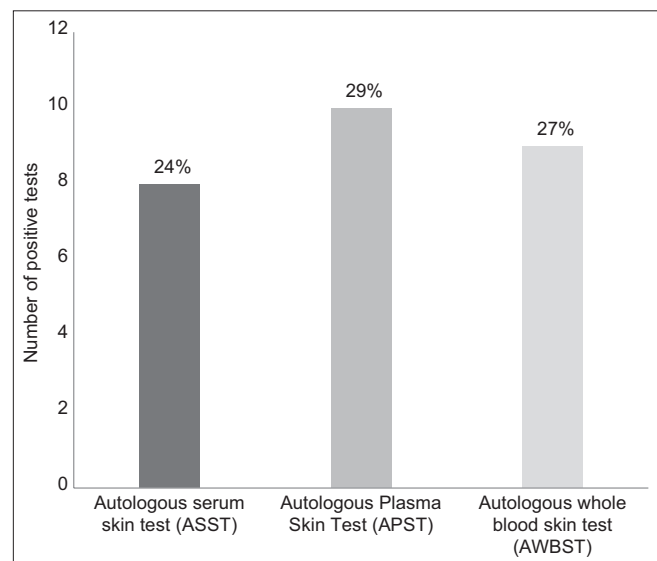


Figure 1: Prevalence of ASST, APST and AWBST positivity in CSU. There were no statistically significant differences between the tests ($P = .86$)

Table 2: Factors associated with autologous skin test positivity

Parameters	Negative test (n=21), n (%) or median (IQR)	Positive test (n=13), n (%) or median (IQR)	P
Age			
20-29	5 (24)	5 (39)	0.64
30-39	9 (43)	4 (31)	
≥40	7 (33)	4 (31)	
Gender			
Males	5 (24)	3 (23)	0.96
Females	16 (76)	10 (77)	
Personal history of atopy	8 (38)	4 (31)	0.66
Family history of atopy	12 (57)	7 (54)	0.85
Associated angio-edema	6 (29)	8 (62)	0.06
Anaphylaxis	0	2 (15)	0.06
Disease duration (month)	30 (33)	12 (38.5)	0.06
Laboratory parameters			
Eos	0.2 (0.4)	0.15 (0.1)	0.39
Plat	319 (80)	291 (72)	0.57
Hb	14.0 (2.4)	13.8 (1.4)	0.92
Total WBC	7.5 (3.1)	6.9 (2.1)	0.29
TSH	1.3 (3.7)	0.9 (1.1)	0.20
Abnormal TSH	1 (5.3)	1 (10)	0.63
Free T4 (FT4)	13.1 (3.7)	12.5 (0.6)	0.33
Complement 3 (C3)	111 (36)	106 (43.1)	0.93
Complement 4 (C4)	24.4 (10.6)	26.4 (7.7)	0.48
ANA positive	2 (10)	1 (8)	0.86
CSU severity			
UAS7	7 (13.5)	17 (15)	0.04*
DLQI	6 (7)	7 (9)	0.68

* $P < 0.05$. Negative test: Patients with negative results to all tests,

Positive test: Patients with positive results to one or more tests. TSH:

Thyroid-stimulating hormone, WBC: White blood cell, Hb: Hemoglobin,

Eos: Eosinophil, Plat: Platelet, IQR: Interquartile range, CSU: Chronic

spontaneous urticarial, UAS7: Urticaria activity score over 7 days, DLQI:

Dermatology Life Quality Index, FT4: Free T4, ANA: Anti-nuclear

antibody

APST positive.^[16] APST generally showed higher positivity rates compared to ASST^[6,14,16,18] but this finding is not always consistent.^[19] A direct comparison of results from various studies is not possible due to the heterogeneity in the materials and methods. The use of sodium citrate for preparation of plasma was introduced in 2006.^[6] Much higher APST positivity rates were observed using sodium citrate anticoagulated plasma instead of heparin^[6,19] as heparin inhibits degranulation of basophils and mast cells.^[6] The result of APST performed using heparinized plasma is less reliable which may account for the inconsistency observed in comparing ASST and APST positivity rates.^[19] Differences in the degree of acceleration, rotational speed, and duration of blood sample centrifugation may be other factors that influence test outcomes.^[4]

Definition of positive test varies with some investigators including the flare reaction.^[20] Consideration of flare or redness was responsible for 52% of positive response in

urticaria patients and 55% of healthy controls.^[21] Cut-off wheal diameter varies from 1.5 mm,^[17,19,22] to 2 mm^[16] and 3 mm.^[6,18] A guideline was introduced in 2009 to standardize ASST procedures and interpretation.^[4] We adhered strictly to the guideline for serum preparation and depended on literatures for plasma and whole blood.^[4,5,16] Our definition of positivity followed EAACI/GA2 LEN Task Force recommendation.^[4]

About a quarter of our patients were positive to at least 1 test. Chronic urticaria can be subdivided into CSU and chronic inducible urticarial (CInU). Etiology for CSU may include autoimmune, idiopathic, allergy, and infection.^[23] Overlap between the etiologies of CSU and CInU is not uncommon.^[23] Autoreactivity occurred only in a proportion of our patients as we diagnose CSU according to the clinical classification and did not subtype the etiology further. It is likely that autoimmune urticaria was not the underlying pathophysiology in most of our study population.

More than half of our patients with positive test were positive to all 3 tests. Differences between positivity rates of ASST, APST, and AWPST were nonsignificant. Our results suggest that all 3 forms of blood/blood components are useful. Whole blood has the advantage of requiring much less equipment, cost, and time for its preparation and administration. It would suit small independent dermatology practices and centers with limited resources. To determine accuracy for each test, however, one will need to extend this study further by testing against normal population.

Factors associated with test positivity

Pretest UAS7 was higher in our patients with at least one positive test ($P = 0.04$). It was not statistically significantly higher when the results of each test were analyzed separately as most patients were positive to all three tests. Urticaria severity and worse effect on the quality of life have been associated with ASST positivity but not APST.^[19] No significant association was observed for both ASST and APST in another study.^[17] Frequency of urticaria episodes was associated with both ASST and APST positivity, however, there were no differences in wheal size, number of wheals, and itch severity between patients with negative compared to positive tests.^[24] There were no other significant factors identified in our cohort. However, history of angioedema, past episode of anaphylaxis, and shorter disease duration were approaching significance in those with positive test. Prick test for indoor, outdoor and food allergens, urticaria duration, and serum IgE are similar between both ASST and APST positive/negative patients.^[18] Most authors investigated the relationship between various parameters with intensity of the test reaction in terms of wheal diameter.

Factors affecting wheal diameter

Mean wheal diameter in our patients correlated positively with TSH level. Thyroid dysfunction is associated with CSU with prevalence ranging from 0% to 54.5%.^[25] Hypothyroidism occurs more commonly than hyperthyroidism. Antithyroid peroxidase antibody is associated with thyroid dysfunction compared to other thyroid autoantibodies.^[26] Thyroid

Table 3: Factors associated with positivity of each skin test

Characteristics	ASST n (%) or median (IQR)		P	APST n (%) or median (IQR)		P	AWBST N (%) or median (IQR)		P	All test+N (%) or median (IQR)		P
	+	-		+	-		+	-		+	-	
	n=8	n=26		n=10	n=24		n=9	n=25		n=7	n=27	
Age (years)												
20-29	4 (50)	13 (50)	0.75	5 (50)	12 (50)	0.60	4 (44)	13 (52)	0.93	4 (44)	13 (52)	0.93
30-39	3 (38)	7 (27)		2 (20)	8 (33)		3 (33)	7 (28)		3 (33)	7 (28)	
≥40	1 (13)	6 (23)		3 (30)	4 (17)		2 (22)	5 (20)		2 (22)	5 (20)	
Gender												
Males	1 (13)	5 (19)	0.66	2 (20)	4 (17)	0.82	2 (22)	4 (16)	0.68	2 (22)	4 (16)	0.68
Females	7 (88)	21 (81)		8 (80)	20 (83)		7 (78)	21 (84)		7 (78)	21 (84)	
Personal history of atopy	2 (25)	5 (19)	0.72	2 (20)	5 (21)	0.96	2 (22)	5 (20)	0.89	2 (22)	5 (20)	0.89
Family history of atopy atopy	6 (75)	16 (62)	0.49	5 (50)	17 (71)	0.25	6 (67)	16 (64)	0.89	6 (67)	16 (64)	0.89
Associated angio-edema	5 (63)	15 (58)	0.81	5 (50)	15 (63)	0.50	6 (67)	14 (56)	0.58	6 (67)	14 (56)	0.58
Anaphylaxis	1 (13)	1 (4)	0.36	1 (10)	1 (4)	0.51	0	2 (8)	0.38	0	2 (8)	0.38
ANA positive	1 (13)	3 (12)	0.94	1 (10)	3 (13)	0.84	1 (11)	3 (12)	0.94	1 (11)	3 (12)	0.94
Abnormal TSH	1 (17)	3 (16)	0.96	1 (13)	3 (18)	0.74	1 (17)	3 (16)	0.96	1 (17)	3 (16)	0.96
Disease duration, (months)	11.5 (17)	12 (20)	0.74	15 (30)	12 (20)	0.78	12 (38)	12 (20)	0.94	12 (20)	12 (20)	0.93
Eos count	0.15 (0.1)	0.2 (0.1)	0.82	0.2 (0.1)	0.2 (0.1)	0.74	0.15 (0.1)	0.2 (0.1)	0.82	0.2 (0.1)	0.2 (0.1)	0.91
Platelet count	290.5 (70.5)	294 (53)	0.79	291 (67)	294 (53)	0.77	309 (50)	294 (55)	0.73	294 (53)	294 (54)	0.81
Hb	14.1 (1.6)	13.8 (1.6)	0.76	13.8 (1.5)	13.8 (1.8)	0.99	13.7 (1.8)	13.8 (1.6)	0.67	13.8 (1.8)	13.8 (1.5)	0.91
WBC count	6.9 (2.4)	6.9 (2.5)	0.89	6.9 (2.3)	6.9 (2.9)	0.99	7 (2.8)	6.9 (2.5)	0.78	6.9 (2.9)	6.9 (2.2)	0.88
TSH	0.90 (2.0)	0.7 (0.5)	0.69	0.9 (0.7)	0.7 (1.2)	0.71	0.7 (1.0)	0.7 (0.8)	0.51	0.7 (1.4)	0.7 (0.7)	0.87
FT4	12.6 (8.6)	12.6 (1.0)	0.64	12.5 (1.0)	12.6 (0.9)	0.48	12.5 (8.8)	12.6 (1.0)	0.93	12.6 (16.5)	12.6 (1.0)	0.67
Complement 3	95.5 (44.6)	104 (45.5)	0.64	112 (50.3)	104 (53)	0.31	101.9 (44.6)	104 (45.5)	0.73	104 (52.3)	104 (41.8)	0.81
Complement 4	23.0 (13.5)	25.9 (12.2)	0.64	26.4 (10.4)	24.3 (16.3)	0.50	25.6 (13.7)	24.3 (12.2)	0.99	24.3 (16.3)	25.1 (10.2)	0.81
UAS7	14 (16)	18 (15)	0.86	18 (16)	17.5 (14)	0.84	17 (14)	18 (15)	0.73	18 (15)	18 (15)	0.74
DLQI	11 (8)	10 (8)	0.77	10 (9)	11 (8)	0.87	7 (9)	13 (8)	0.67	13 (8)	9 (8)	0.74

TSH: Thyroid-stimulating hormone, WBC: White blood cell, Hb: Hemoglobin, Eos: Eosinophil, Plat: Platelet, IQR: Interquartile range, CSU: Chronic spontaneous urticarial, UAS7: Urticaria activity score over 7 days, DLQI: Dermatology Life Quality Index, FT4: Free T4, ANA: Anti-nuclear antibody

Table 4: Correlations between mean skin test wheal diameter at 30 min with clinical characteristics and chronic spontaneous urticaria severity in patients with positive autologous skin test

Parameters	Wheal diameter (n=13)	
	r	P
Age	-0.19	0.53
Duration of CSU	0.26	0.40
Eos	-0.19	0.55
Hb	-0.20	0.53
Plat	-0.24	0.46
WBC	0.21	0.50
TSH	0.66	0.039*
FT4	-0.24	0.51
C3	-0.33	0.29
C4	-0.38	0.23
Baseline UAS7	-0.12	0.69
Baseline DLQI	-0.44	0.13

* $P < 0.05$. CSU: Chronic spontaneous urticarial, TSH: Thyroid-stimulating hormone, WBC: White blood cell, Hb: Hemoglobin, Eos: Eosinophil, Plat: Platelet, UAS7: Urticaria activity score over 7 days, DLQI: Dermatology Life Quality Index, FT4: Free T4

antibodies occur in 0%–53.6% of CSU patients, the prevalence varies according to the type of antibody tested.^[25] However, not all patients with thyroid autoantibodies have laboratory and clinical evidence of thyroid dysfunction. Antithyroid peroxidase antibody and high TSH are predictors for the development of hypothyroidism.^[27] Two of our patients had low TSH. We did not investigate for thyroid autoimmunity; a systematic review showed that results are inconsistent for the association of autoantibodies with thyroid dysfunction, CSU severity, and ASST positivity.^[25]

Tests' wheal diameter/intensity of response have been associated with a history of angioedema, ANA positivity,^[16] females and older age^[17] for both ASST and APST. We did not find significant correlation between positive test with age, disease duration, laboratory parameters, and DLQI. Wheal diameter is most likely not related to disease severity.^[16]

Skin test positivity as a prognostic factor

Patients with positive APST needed higher doses of antihistamine compared to those with negative APST while there were no differences in antihistamine requirement between ASST positive or negative patients.^[24] Two-year disease remission rate was observed to be 5 times higher in patients with negative test compared to those positive to both ASST and APST.^[20] Remission rate was not influenced by positivity to ASST or APST alone.^[20] Severity of CSU in relation to test positivity has been described above.

Therapeutic potential of autologous whole blood for skin testing and other autologous skin tests

Intramuscular injections of autologous serum and whole blood (autohemotherapy) have been successfully used in the treatment of CSU.^[5,28-31] Therapeutic results were better

in patients with positive ASST.^[28] Intramuscular therapy is performed weekly for 8–10 weeks^[28-31] and 9 weeks for subcutaneous therapy.^[32] Autologous skin tests itself may have a therapeutic role. DLQI ($P = 0.03$) and UAS7 ($P = 0.04$) improved 8-week posttests, however, but this requires further investigation and confirmation. Majority of our patients had mild CSU which is a limitation of the study. Inclusion of more patients with severe CSU may produce better results. Recruitment was difficult as most patients with severe CSU were unable to withhold antihistamine before the skin tests due to intolerable itch.

CONCLUSION

In conclusion, about a quarter of CSU patients demonstrated autoreactivity. There were no significant differences in skin test responses with ASST, APST, and AWBST. Half of the patients with positive test were positive to all three tests. All autologous tests including serum, plasma, and whole blood may be utilized in CSU, especially in centers with limited resources. Autologous skin testing may be useful for predicting CSU severity early in the course of the disease.

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Conflicts of interest

There are no conflicts of interest.

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