Original Article

Serum Amyloid A as a Potential Biomarker for Disease Activity in Chronic Spontaneous Urticaria

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What is already known about this topic? Serum amyloid A (SAA) levels are higher among patients with chronic urticaria. However, no studies have assessed SAA levels in chronic spontaneous urticaria (CSU) or its correlation with Urticaria Activity Score over 7 days (UAS7).

What does this article add to our knowledge? This research shows that SAA correlates with UAS7 with more strength than C-reactive protein and is higher among patients with controlled CSU than in patients with noncontrolled CSU as well as in those with concomitant angioedema or delayed pressure urticaria.

How does this study impact current management guidelines? SAA might be a useful tool for assessing disease activity in patients with CSU.

BACKGROUND: Chronic spontaneous urticaria (CSU) is an inflammatory skin disease with a complex physiopathology. Serum amyloid A (SAA), an acute-phase reactant, has been proposed as a potential biomarker in urticaria but has yet to be studied in a population with CSU or correlated with disease activity as indicated by the Urticaria Activity Score summed over 7 days (UAS7).

OBJECTIVE: We sought to determine SAA-1 levels in patients with CSU and correlate them with its activity and control, as well as with clinical features of CSU and other potential blood biomarkers.

METHODS: We conducted a retrospective multicenter study of 67 patients with CSU, from whom we obtained demographic and clinical data, UAS7 as an indicator of CSU activity, and blood and serum markers.

RESULTS: SAA-1 levels positively correlated with UAS7 ($r_s = 0.47$, $P < .001$). SAA-1 levels were higher in patients with noncontrolled (UAS7 > 6) CSU than in those with controlled (UAS ≤ 6) CSU ($P < .001$) and were also higher in patients with concomitant angioedema ($P = .003$) or delayed pressure urticaria ($P = .003$).

CONCLUSION: We propose SAA-1 as a potential biomarker for activity in CSU. Further studies are required to evaluate its potential role as a biomarker for other CSU outcomes, such as response to treatment. © 2023 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy,

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Abbreviations used
CIndU- Chronic inducible urticaria
CRP- C-reactive protein
CSU- Chronic spontaneous urticaria
DPU- Delayed pressure urticaria
IQR- Interquartile range
nsAH- Nonsedating H1-antihistamine
SAA- Serum amyloid A
UAS7- Urticaria Activity Score summed over 7 consecutive days

Key words: *Chronic urticaria; Chronic spontaneous urticaria; Serum amyloid A protein; Biomarkers; Urticaria*

Chronic spontaneous urticaria (CSU) is an inflammatory skin disease defined as the presence of wheals with or without angioedema for more than 6 weeks without an identifiable cause.[1] Several clinical, immunological, and inflammatory biomarkers have been proposed as biomarkers related to disease activity and response to treatment in patients with CSU.[2-5] Among these are acute-phase reactants such as C-reactive protein (CRP) and D-dimer, both of which are related to CSU activity,[4-10] as well as response to nonsedating H1-antihistamines (nsAHs).[5,8-11] D-dimer has also been explored as a potential biomarker for response to omalizumab, but results have been inconclusive,[12-14] unlike total serum IgE, which correlates with omalizumab response.[5] To date, there is no consensus on a reliable biomarker that can be used for decision-making in patients with CSU.

Recently, other molecules have been suggested as potential biomarkers for CSU. Such is the case for serum amyloid A (SAA), a known acute-phase reactant that has been identified as an activity biomarker for rheumatoid disease[15] and is commercially available for use in a clinical setting. SAA is an acute-phase apolipoprotein primarily synthesized by the liver in response to inflammation, and SAA-1 is the major isoform.[16,17] Its role in urticaria has been scarcely explored, with evidence of higher levels of SAA in patients with acute urticaria and moderate-severe chronic urticaria,[18] as well as in those with a longer wheal duration.[19] However, no studies to date have explored SAA levels in a population with CSU or their correlation with the Urticaria Activity Score summed over 7 consecutive days (UAS7) or with other potential CSU activity biomarkers, such as D-dimer. The aim of this study was to explore the relationship between SAA-1 levels and disease activity in patients diagnosed with CSU and their correlation with other proposed biomarkers.

METHODS

Study design and setting

We conducted a cross-sectional multicenter study of 67 patients diagnosed with CSU who were retrospectively included from a patient database. The data of these patients were collected from the allergy departments of 5 hospitals between January 2014 and December 2022. Samples included in the study were provided by the Biobank of the University of Navarra and were processed following standard operating procedures approved by the ethical and scientific committees.

Participants

Patients were recruited from the allergy departments of Clínica Universidad de Navarra (Pamplona, Spain), Complexo Hospitalario Universitario A Coruña (A Coruña, Spain), Hospital General Universitario Gregorio Marañón (Madrid, Spain), Hospital Universitari Vall d'Hebron (Barcelona, Spain), and Hospital Universitari Joan XXIII (Tarragona, Spain). Approval was obtained from the ethics committee of each collaborating center. Patients were included if they met all the following criteria: (1) a diagnosis of CSU (defined as the presence of wheals with or without angioedema over >6 weeks, without an identifiable cause) established by an allergy specialist and (2) age ≥18 years. Exclusion criteria were (1) having isolated chronic inducible urticaria (CIndU), (2) having taken systemic corticosteroids in the previous week, and (3) having taken immunosuppressant or biological drugs in the previous 3 months. CSU patients with associated CIndU were not excluded from the study. In most cases, the patients recorded their angioedema events and reported them in a follow-up visit; however, in some cases, the diagnosis was made due to past events.

Data collection

Demographic and clinical features, as well as CSU characteristics and activity scores, were retrospectively obtained from medical records at each collaborating center. Blood and serum samples, collected as part of routine clinical care and stored for past research or future investigation, were available from all patients, and serum samples were stored at −80°C. Measurements for blood counts and blood/serological marker levels, including CRP, D-dimer, and total IgE levels, were performed in each clinical laboratory center. SAA-1 levels were measured at each center if possible or by commercial ELISA (R&D Systems, Minnesota) when necessary.

CSU activity was determined by the UAS7, which is the sum of the Urticaria Activity Scores determined over 7 consecutive days, ranging from 0 (lowest activity) to 42 (highest activity).[1] The UAS7 evaluates daily wheal and pruritus appearance and quantity, as reported by the patient. The UAS7 was obtained from the week before clinical evaluation and blood sampling. Patients with CSU were then classified according to their UAS7 as having controlled (UAS7 ≤ 6) or noncontrolled (UAS7 > 6) CSU. This UAS7 cutoff was chosen according to its use as an endpoint in clinical trials, good correlation with quality-of-life scores, and recommendation by recent guidelines.[20,21]

All patients underwent treatment with nsAHs during the study period, according to guideline recommendations.[1] The nsAHs used by the study patients were as follows: cetirizine, levocetirizine, loratadine, desloratadine, fexofenadine, mizolastine, ebastine, or bilastine. Data on nsAH dose and frequency were collected, and patients were identified as taking therapeutic or supratherapeutic doses (up to 4-fold the therapeutic dose). Patients who had taken systemic corticosteroids in the previous week were excluded from the study; likewise, patients who had received immunosuppressant or biological drugs, such as omalizumab, in the previous 3 months were excluded.

Statistical analysis

Study variable data were tested for normality using the Shapiro-Wilk test. Qualitative variable data are presented as frequencies and percentages, and quantitative variable data are presented as means and standard deviations or medians and interquartile ranges (IQRs), according to a variable data distribution. Qualitative variables were compared using the χ^2 test or the Fisher exact test.

TABLE I. Characteristics of patients with controlled (UAS7 $\leq$ 6) and noncontrolled (UAS7 > 6) CSU

Characteristics	Noncontrolled CSU (n = 47)	Controlled CSU (n = 20)	*P* value
Age, mean (SD) (y)	50.7 (14.7)	51.4 (12.2)	.862
Sex (female), n (%)	31 (65.9)	12 (60.0)	.642
Presence of angioedema, n (%)	38 (80.9)	16 (80.0)	.936
Presence of CIndU, n (%)	26 (55.3)	6 (30.0)	.058
Dermographism	10 (21.3)	2 (10.0)	.271
Delayed pressure urticaria	19 (40.4)	3 (15.0)	**.043**
Cold urticaria	1 (2.1)	0 (0.0)	.511
Cholinergic urticaria	0 (0.00)	1 (5.0)	.122
Aquagenic urticaria	1 (2.1)	0 (0.0)	.511
SAA-1 (μg/L), median (IQR)	11.7 (2.8-32.0)	1.7 (0.7-4.5)	**<.001**
D-dimer (ng/mL), median (IQR)	644 (450-1487)	270 (175-391)	**<.001**
CRP (mg/dL), median (IQR)	0.7 (0.2-1.2)	0.2 (0.1-0.4)	**<.001**
Blood eosinophils ($\times 10^3/mm^3$), median (IQR)	0.11 (0.03-0.16)	0.12 (0.10-0.17)	.538
Blood basophils ($\times 10^3/mm^3$), median (IQR)	0.01 (0.01-0.03)	0.03 (0.01-0.06)	.177
Total IgE (kU/L), median (IQR)	57.6 (10.5-188.5)	103.4 (48.0-197.0)	.132

Bold values indicate statistical significance ($P < .05$). Qualitative variables were compared by using the χ^2 test or the Fisher exact test. Comparative analyses for quantitative variable were conducted using the Student *t* test or analysis of variance when the variables were normally distributed and the Wilcoxon rank-sum or Kruskal-Wallis test when the variables were not normally distributed.

CIndU, Chronic inducible urticaria; *CRP*, C-reactive protein; *CSU*, chronic spontaneous urticaria; *IQR*, interquartile range; *SAA-1*, serum amyloid A-1; *SD*, standard deviation; *UAS7*, sum of the Urticaria Activity Scores over 7 consecutive days.

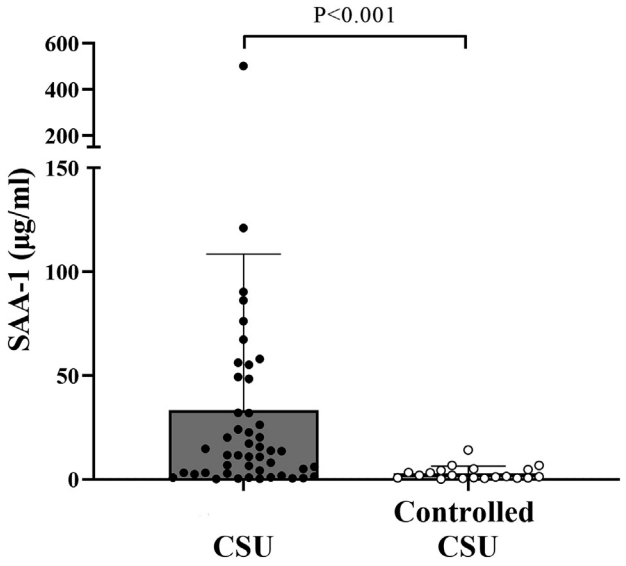

FIGURE 1. Comparison of SAA-1 levels between patients with controlled (UAS $\leq$ 6) and noncontrolled (UAS7 > 6) CSU. Groups were compared with the Mann-Whitney test. The *P* value is shown in the figure. *CSU*, Chronic spontaneous urticaria; *SAA-1*, serum amyloid A-1; *UAS7*, sum of the Urticaria Activity Scores over 7 consecutive days.

Comparative analyses for quantitative variable data with a normal distribution were conducted using the Student *t* test for comparisons of 2 groups and analysis of variance for comparisons of more than 2 groups. Comparative analyses for quantitative variable data without a normal distribution were conducted using the Wilcoxon rank-sum test for comparisons of 2 groups and the Kruskal-Wallis test for comparisons of more than 2 groups. Correlations between quantitative variables were analyzed with the Pearson correlation coefficient or the Spearman rank correlation coefficient, according to the variable data distribution. Differences of $P < .05$ were considered to be statistically significant. Statistical analyses were conducted using the Stata/MP 14.2 software (Stata Corp, College Station, Texas), and figures were created with GraphPad Prism 9 (GraphPad Software, San Diego, Calif).

RESULTS

Patient characteristics

Sixty-seven patients diagnosed with CSU were included in the study, with a mean age of 50.9 $\pm$ 1.8 years. Forty-three patients (64.2%) were female, and 24 (35.8%) were male. The presence of angioedema was reported by 54 patients (80.6%), and 32 patients (47.8%) presented with an associated CIndU. Among them, delayed pressure urticaria (DPU) was the most prevalent CIndU (32.8%), followed by dermographism (17.9%). Five patients (7.5%) presented with more than 1 concomitant CIndU. All patients were undergoing treatment with nsAHs; 17 patients (25.4%) were taking therapeutic doses, whereas 50 (74.6%) were using supratherapeutic doses. Of those taking supratherapeutic nsAH doses, 22 (32.8%) were taking 2-fold doses, 17 (25.4%) 3-fold doses, and 11 (16.4%) 4-fold doses.

CSU activity

A detailed description of the clinical characteristics of patients with controlled and noncontrolled CSU is shown in Table I. Twenty patients (29.9%) were classified as having controlled CSU (UAS7 $\leq$ 6), whereas the rest (70.1%) were classified as having noncontrolled CSU (UAS7 > 6). The median UAS7 was 2 (IQR: 0-4) among patients with controlled CSU and 31 (IQR: 21-37) among patients with noncontrolled CSU ($P < .001$). Only 6 (9.0%) patients were urticaria free (UAS7 = 0). Age, sex, presence of angioedema, and presence of CIndU were not associated with CSU control. There were a higher proportion of patients with DPU in the group with noncontrolled CSU (40.4%) than in the group with controlled CSU (15.0%,

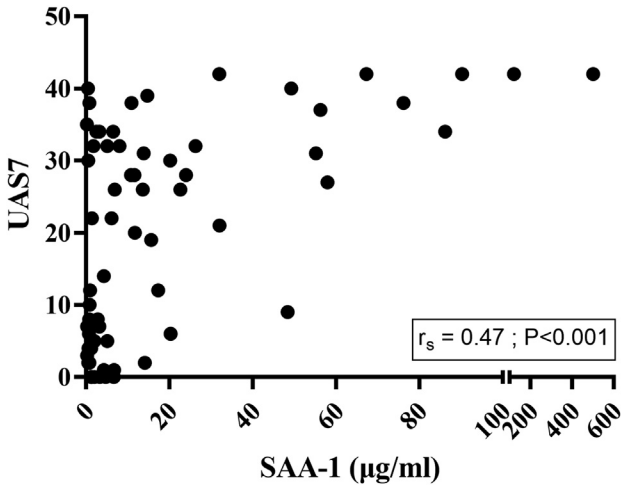

FIGURE 2. Correlation between SAA-1 levels and UAS7 in patients with CSU. Spearman's rank correlation coefficient (r_s) is shown in the figure, along with the *P* value. *CSU*, Chronic spontaneous urticaria; *SAA-1*, serum amyloid A-1; *UAS7*, sum of the Urticaria Activity Scores over 7 consecutive days.

TABLE II. Correlation between blood parameters and UAS7 in patients with CSU

Parameters	r_s	*P* value
SAA-1	0.47	**<.001**
D-dimer	0.6	**<.001**
CRP	0.39	**.001**
Blood eosinophils	−0.26	.106
Blood basophils	−0.19	.249
Total IgE	−0.18	.164

Spearman's rank correlation coefficient (r_s) was used due to the variable data distribution.
Bold values indicate statistical significance ($P < .05$).
CRP, C-reactive protein; *CSU*, chronic spontaneous urticaria; *SAA-1*, serum amyloid A-1; *UAS7*, sum of the Urticaria Activity Scores over 7 consecutive days.

$P = .043$); however, UAS7 were not significantly different between patients with and without DPU ($P = .111$) or between patients with any other CIndU subtype.

The mean nsAH dose among patients with controlled CSU was 1.3 ± 0.6 times the therapeutic dose, compared with 2.7 ± 0.9 times the therapeutic dose among patients with noncontrolled CSU. Of the 17 patients taking therapeutic doses, 82.4% had controlled CSU. In contrast, only 6 of the 50 (12%) patients taking supratherapeutic doses had controlled CSU. The rates of controlled CSU among the different supratherapeutic dose groups were as follows: 22.7% among those taking 2-fold doses and 5.9% among those taking 3-fold doses. None of the 11 patients who had been taking 4-fold nsAH doses had controlled CSU. Median UAS7 according to nsAH doses were as follows: 1.2 (IQR: 0.7-3.3) among those taking therapeutic doses, 6.8 (IQR: 1.4-24.0) among those taking 2-fold doses, 10.8 (IQR: 3.2-26.3) among those taking 3-fold doses, and 20.2 (IQR: 6.5-49.2) among those taking 4-fold doses ($P = .003$). The nsAH dose showed a moderate positive correlation ($r_s = 0.66$, $P < .001$) with UAS7.

TABLE III. Correlation matrix for blood parameters in patients with CSU

Variable	1	2	3	4	5	6
SAA-1	–					
D-dimer	**0.63**	–				
CRP	**0.70**	**0.50**	–			
Blood eosinophils	−0.21	−0.23	−0.22	–		
Blood basophils	**−0.38**	**−0.42**	**−0.41**	0.27	–	
Total IgE	**−0.28**	**−0.38**	−0.15	**0.33**	0.28	–

Spearman's rank correlation coefficient (r_s) was used due to the variable data distribution.
Bold values indicate statistical significance ($P < .05$).
CRP, C-reactive protein; *CSU*, chronic spontaneous urticaria; *SAA-1*, serum amyloid A-1.

SAA-1 and CSU

SAA-1 levels were higher among patients with noncontrolled CSU (11.7 [IQR: 2.8-32.0] µg/mL) than among those with controlled CSU (1.7 [IQR: 0.7-4.5] µg/mL, $P < .001$), as shown in Figure 1. SAA-1 levels showed a moderate positive correlation with UAS7 ($r_s = 0.47$, $P < .001$), as shown in Figure 2.

SAA-1 levels were not associated with age ($P = .820$) or sex ($P = .147$). SAA-1 levels were higher in patients with angioedema (9.4 [IQR: 2.0-24.0] µg/mL) than in those without angioedema (0.8 [IQR: 0.6-3.3] µg/mL, $P = .003$). SAA-1 levels were also higher in patients with DPU (14.7 [IQR: 6.5-48.3] µg/mL) than in those without DPU (3.2 [IQR: 0.8-11.7] µg/mL, $P = .003$). SAA-1 levels among patients with other subtypes of CIndU were not significantly different. SAA-1 levels among patients with 2 simultaneous CIndU subtypes were higher than those among patients with only 1 CIndU subtype (48.3 [IQR: 15.6-76.2] µg/mL vs 6.9 [IQR: 0.8-24.0] µg/mL, respectively), although this difference did not reach statistical significance ($P = .052$).

Other biomarkers and CSU

Correlation coefficients between blood parameters and UAS7 can be seen in Table II. D-dimer levels were higher in patients with noncontrolled CSU (644 [IQR: 450-1487] ng/mL) than in patients with controlled CSU (270 [IQR: 175-391] ng/mL, $P < .001$). CRP levels were also higher among patients with noncontrolled CSU (0.7 [IQR: 0.2-1.2] mg/dL) than among patients with controlled CSU (0.2 [IQR: 0.1-0.4] mg/dL, $P = .008$). CRP levels were higher in CSU patients with angioedema (0.6 [IQR: 0.2-1.1] mg/dL) than in those without angioedema (0.2 [IQR: 0.1-0.4] mg/dL, $P = .046$). CRP levels were also higher among patients with DPU (0.8 [IQR: 0.3-2.2] mg/dL) than among those without (0.3 [IQR: 0.2-0.9] mg/dL, $P = .020$). D-dimer levels were not significantly different between patients with and without angioedema or any CIndU subtype. UAS7 showed a moderate positive correlation with D-dimer levels ($r_s = 0.60$, $P < .001$) and a weak positive correlation with CRP levels ($r_s = 0.39$, $P = .001$). No statistically significant correlations were found between eosinophil counts, basophil counts or total IgE levels, and UAS7.

Correlation between biomarkers

Correlations between all evaluated blood parameters are shown in Table III. SAA-1 levels showed a strong positive correlation with CRP levels ($r_s = 0.70$, $P < .001$) and a moderate positive correlation with D-dimer levels ($r_s = 0.63$, $P < .001$). D-dimer

and CRP levels showed a moderate positive correlation with each other ($r_s = 0.50$, $P < .001$). Total IgE levels were negatively correlated with SAA-1 ($r_s = -0.28$, $P = .027$) and D-dimer ($r_s = -0.38$, $P = .040$) levels; no statistically significant correlation between CRP levels and total IgE levels was found. Basophil counts showed a weak negative correlation with SAA-1 levels ($r_s = -0.38$, $P = .018$) and a moderate negative correlation with D-dimer ($r_s = -0.42$, $P = .010$) and CRP levels ($r_s = -0.41$, $P = .010$) but not with total IgE levels. Eosinophil counts showed a weak positive correlation with total IgE levels ($r_s = 0.32$, $P = .046$) but not with SAA-1, D-dimer, or CRP levels.

DISCUSSION

CSU is a common entity that significantly impacts quality of life.[1] With the arrival of new therapies for CSU, such as Bruton's tyrosine kinase inhibitors and anti-Kit receptor monoclonal antibodies,[22] it is becoming more important to phenotype the disease to facilitate the selection of an evidence-based and personalized treatment.[23,24] Moreover, our aim should be to achieve complete CSU control, as recommended by recent guidelines.[1] Paradoxically, there is a lack of consensus on the definition of control in CSU.[25] Thus, it is essential to have reliable, reproducible, and well-correlated biomarkers at hand.

Acute-phase reactants are natural candidates for this role due to their release in response to numerous inflammatory mechanisms, which are part of the physiopathology of CSU. In the present study, we explored SAA-1 in a population with CSU and compared its levels with several disease characteristics, including activity and disease control as indicated by the UAS7, and we explored the correlation of SAA-1 levels with the levels of other potential biomarkers such as CRP and D-dimer. Our findings portray SAA-1 as a potential biomarker for CSU activity, which needs to be further explored.

Previously, Lu et al[18] found higher levels of SAA in patients with acute and moderate-severe urticaria than in healthy controls. However, the UAS was determined over 4 days instead of 7 and categorized for subsequent comparisons. The correlation between UAS and SAA levels was not performed. Our findings show that SAA-1 positively and moderately correlates with UAS7, which is the recommended scoring system for indicating activity in CSU.[1] When categorizing patients with CSU according to their UAS7 into controlled and noncontrolled CSU groups, SAA-1 levels were also significantly higher in the noncontrolled CSU group. UAS7 correlated with SAA-1 with more strength than with CRP. Thus, SAA-1 might be a more reliable and sensitive marker of disease activity than CRP, which has been previously suggested regarding other pathologies,[15,17] although this would require confirmation by studies with a larger number of patients.

There is a rationale for the observed relationship between SAA and CSU. SAA levels increase up to 1000-fold in response to inflammation, and its transcription is upregulated by proinflammatory cytokines such as interleukin (IL)-1β, IL-6, and tumor necrosis factor-α, with synergistic effects.[26,27] IL-6 plays an important role in SAA induction, as SAA mRNA expression is inhibited by IL-6 receptor blockade.[27] These cytokines are more highly expressed in patients with CSU, and IL-6 and tumor necrosis factor-α levels correlate with CSU activity.[28] More so, SAA has a chemoattractant effect on mast cells[29] as well as on neutrophils and T cells.[30] SAA may also play a role in type 2 immunity by participating in the activation of type 2 innate lymphoid cells.[31] Thus, SAA seems to be actively involved in these inflammatory pathways, which might explain its observed correlation with disease activity in patients with CSU.

SAA, as is the case with CRP, reflects the chronic inflammation present in CSU. This is in line with our findings of higher levels of SAA-1 among CSU patients with concomitant angioedema, as well as in those with concomitant DPU. CRP levels were also higher in these 2 groups, but not D-dimer levels, which are more a reflection of extrinsic coagulation activation, although they can also be related to the inflammatory response.[32] The presence of angioedema in CSU has been linked to a longer disease duration,[33] whereas concomitant CIndU has been related to higher disease activity.[34] We found no difference in UAS7 between patients with and without concomitant DPU or any other CIndU subtype. However, CSU patients with UAS7 > 6 were more likely to have DPU (40%) than those with UAS7 ≤ 6 (15%). Previously, Curto-Barredo et al[34] compared disease activity in patients with isolated CSU and patients with CSU with concomitant CIndU and found no difference in UAS7 between these groups. However, when calculating the sum of UAS over 3 consecutive weeks, these were higher in CSU patients with concomitant CIndU. SAA-1 levels might be able to reflect the underlying chronic inflammation that characterizes CSU, particularly in patients with concomitant CIndU. In support of this idea, SAA-1 levels were higher in patients with 2 or more concomitant CIndUs than in those with 1 CIndU, although this difference did not reach statistical significance.

In accordance with previous studies,[4-10] CRP and D-dimer levels in our population were associated with CSU activity and were significantly higher among patients with noncontrolled CSU. Both acute-phase reactants also correlated with moderate-severe strength with SAA-1. As mentioned before, D-dimer and SAA-1 showed stronger correlations with CSU activity than CRP. This might suggest a deeper involvement of SAA-1 in the physiopathology of CSU, as seems to be the case with D-dimer, which reflects the dysregulation of blood coagulation and fibrinolysis pathways present in some patients with CSU.[28] D-dimer levels also parallel the clinical response to omalizumab,[12] although baseline determinations do not predict response to this treatment.[13,14] Total serum IgE levels correlate with response to omalizumab, with lower levels in those with poor or no response.[5] In our study, total IgE levels negatively correlated with SAA-1, as well as D-dimer. This could suggest a link between higher levels of SAA-1 and a lower response to omalizumab, which would need to be evaluated by future studies. Until more data are gathered on SAA-1, we do not have a basis to use SAA-1 as a decision-making biomarker or for the differential diagnosis of CSU from other urticarial rash.

Whether SAA-1 might behave in a similar manner to D-dimer regarding the course and response to treatment of CSU remains unexplored, and further studies are warranted to determine SAA-1 levels at baseline and after treatment with nsAHs and omalizumab. Likewise, it should be prospectively explored whether these increased SAA-1 levels in patients with CSU might evolve toward glomerular amyloid deposition. Although serum SAA-1 levels do not seem to correlate with amyloid deposits in other chronic inflammatory disorders such as rheumatoid diseases,[15] this should also be investigated in CSU, particularly in patients with prolonged and severe disease.

Our study had some limitations. As patients were retrospectively included, some variables had missing data. The study was

cross-sectional and noninterventional, so we were unable to evaluate response to treatment as an outcome. The study was conducted in centers of reference for the diagnosis and management of chronic urticaria, so there could be an overrepresentation of severe cases of CSU and the frequency of some of its clinical features, such as the presence of angioedema. Our study population was small, which could limit the significance of some of our findings.

CONCLUSION

This study proposes SAA-1 as a novel biomarker for the activity of CSU as measured by UAS7. Further longitudinal studies are warranted to determine the extent of its involvement and long-term consequences in the physiopathology of CSU, as well as its potential role as a predictor of other outcomes such as response to treatment with nsAHs, omalizumab, and other emergent therapies.

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