Original Article

Prevalence of Inducible Urticaria in Patients with Chronic Spontaneous Urticaria: Associated Risk Factors

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What is already known about this topic? Chronic urticaria significantly affects patients' quality of life. The identification of possible physical triggers could obviate lifestyle restrictions and improve clinical control.

What does this article add to our knowledge? Environmental factors such as geographical characteristics could play a role in the development of some types of inducible urticaria, whereas atopy and self-reactivity are major risk factors for spontaneous urticaria.

How does this study impact current management guidelines? Most patients avoid physical stimuli that might be triggers of urticaria. Physical triggers must be verified by challenge tests to avoid unnecessary lifestyle restrictions.

BACKGROUND: Information on the prevalence of inducible urticaria (IU) in patients with chronic spontaneous urticaria (CSU) and the factors affecting this prevalence is scarce in the literature.
OBJECTIVES: To estimate the frequency of IU in patients with CSU and to explore possible factors associated with CSU.
METHODS: Patients older than 12 years diagnosed with CSU and a control group with no history of urticaria were recruited from 2 different cities. All patients were questioned about triggers associated with exacerbation of urticaria, and challenge tests were performed for symptomatic dermographism, pressure, cold, water, and exercise. Atopy to mites and self-reactivity to autologous serum were evaluated using skin tests.
RESULTS: The study population comprised 245 patients with CSU and 127 controls. Of the patients with CSU, 186 (75.9%) reported a physical trigger, although only 89 (36.3%) had a positive challenge test result. The challenge tests showed that symptomatic dermographism was the most common type of IU, affecting 24.8% of the CSU group, followed by cold, which affected 13.4%. In the control group, 3.9% of patients were positive for symptomatic dermographism. People living in Medellín city had a higher frequency of symptomatic dermographism 28.5% (odds ratio, 2.1; 95% CI, 1-4.4; $P = .03$) and cold urticaria 16.5% (odds ratio, 3.3; 95% CI, 1.125-9.8; $P = .02$) than did people living in Bogotá (dermographism 14.4% and cold 5.2%). Atopy and self-reactivity were more frequent in patients with CSU than in the control group.
CONCLUSIONS: Physical triggers must be verified by challenge tests to avoid unnecessary lifestyle restrictions. Environmental factors such as geographical characteristics could play a key role in the development of some types of IU, whereas atopy and self-reactivity are major risk factors for CSU. © **2016 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;5:464-70)**

Key words: *Atopy; Self-reactivity; Cold; Exercise; Friction; Dermographism; Pressure; Water; Urticaria*

Urticaria comprises a heterogeneous group of diseases that are common in the general population[1] and have a major impact on quality of life. Chronic urticaria (hives and/or angioedema for more than 6 weeks) is estimated to affect between 0.5% and 5% of the general population.[2,3] Chronic spontaneous urticaria (CSU) and inducible urticaria (IU) are the most common types of chronic urticaria and may occur simultaneously or independently. CSU occurs spontaneously with no apparent trigger. IU occurs when the formation of hives is reproducible after a specific stimulus, for example, a mechanical stimulus (friction, pressure, and vibration), thermal stimulus (cold, heat), aquagenic stimulus (water), and electromagnetic stimulus (solar radiation).[4] In a recent meta-analysis,[5] the prevalence of IU was estimated at 13.1% to 14.9% among patients with chronic urticaria. This prevalence is low compared with that reported from other

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Abbreviations used
CSU- Chronic spontaneous urticaria
IU- Inducible urticaria

studies,[6,7] suggesting that results must be interpreted by taking into consideration the methodology used (self-reporting or challenge testing). Outcome can be affected by various factors. The clinical relevance of physical triggers is very important, especially in patients with CSU, where hives and angioedema can occur even without exposure to an inducible stimulus; therefore, mistakes in the identification of triggers lead to unnecessary restrictions that significantly affect quality of life.

Several conditions, including autoimmune diseases and systemic infections and specific drugs, have been associated with urticaria exacerbations. In some cases, the chronicity of the disease could be explained by molecular mimicry; however, to our knowledge, no data have been reported on environmental conditions (eg, temperature and humidity) that affect the onset and prevalence of IU. In addition, information about the role of atopy and self-reactivity in the development of chronic urticaria is controversial.

In this study, we evaluated the frequency of IU in patients diagnosed with CSU on the basis of self-reporting and challenge testing with 5 physical triggers. We also evaluated whether environmental and immunological factors could act as potential risk factors for IU and CSU.

METHODS

Study population

We performed a multicenter, prospective, descriptive study from August 2013 to December 2014. The study population came from a previously formed cohort (URTICA: Urticaria Research of Tropical Impact and Control Assessment, ClinicalTrials.gov number: NCT01940393).[8] Because the aim of the study was to evaluate whether inhibition of the skin test wheal correlated with the clinical effect of antihistamines, patients with baseline inhibition of the cutaneous response to histamine (wheal <3 mm) were not included. The CSU group included patients older than 12 years with chronic urticaria, which was defined as the recurrence of hives, with or without angioedema, on more than 3 days per week and persisting for at least 6 weeks. The disease was diagnosed by an allergist or dermatologist. The exclusion criteria included the following: systemic disease that could explain the hives; systemic corticosteroids during the 3 weeks before recruitment; immune deficiency, dermatitis, and/or any other disease that could alter the results of the skin test; and compromised immune system because of the risk of secondary acute urticaria by infection. We also excluded pregnant women, patients with physical or mental disabilities, people with decompensated cardiovascular disease, and people with a chronic disease that could compromise the patient during challenge testing.

The control group consisted of people older than 12 years with no history of chronic urticaria or history of acute urticaria in the previous 2 years. The control group was evaluated by a physician before enrollment.

We used the *Dermatology Life Quality Index* (DLQI) because it had previously been validated in Colombia. We also used the *Urticaria Activity Score* (UAS) to measure disease severity.

Demographic characteristics

Patients and controls were recruited from 2 cities in Colombia (Bogotá and Medellín) with different environmental characteristics. The genetic background of both populations is very similar and results from a racial admixture between native Americans, Spaniards, and (albeit less frequently) Africans (<10.9%).[9,10] The environmental characteristics of the cities are different: Medellín is located in the Aburra Valley area (6° 14′ 41″ North, 75° 34′ 29″ West), 1479 meters above sea level, with an average annual temperature of 22°C and relative humidity of 66%. Bogotá (4° 35′ 56″ North, 74° 04′ 51″ West) is located 2640 meters above sea level, with an average annual temperature of 14°C and relative humidity of 76%.

Allergen skin test and autologous serum and plasma skin test

IgE sensitization was evaluated using the prick test according to international guidelines[11] with extracts for *Blomia tropicalis*, *Dermatophagoides pteronyssinus*, and *Dermatophagoides farinae*, which are the principal allergens in this region.[12-14] We also evaluated sensitization to foods that the patient associated with exacerbation. Patients with atopy for environmental or dietary allergens received recommendations on avoidance.

Self-reactivity was evaluated using the autologous serum skin test and autologous plasma skin test according to international guidelines. Briefly, 0.05 mL of serum and 0.05 mL of plasma were injected intradermally. Histamine was used as a positive control and saline solution as a negative control. A wheal of 1.5 mm over the negative control after 30 minutes was considered a positive result.[15] European and international guidelines recommend serum over plasma[15]; however, we performed both tests with the same methodology to compare results.

Study design and challenge test

The study design is presented in Figure 1. All participants underwent a complete physical examination before their challenge tests, and the triggers identified by patients were recorded in their clinical history. The physicians performing the challenge test were familiar with the patients' clinical history. In all patients, challenge tests were performed for the 5 most common triggers (dermographism, cold, exercise, water, and pressure). Challenge tests were completed under similar environmental conditions. Patients were acclimated to the challenge room temperature for at least 30 minutes before testing. At least 1 week before the challenge tests, all the patients refrained from taking antihistamines or any other drug that could affect the outcome of the challenge tests. Once the challenge tests were complete, all the participants remained under observation for a period of 2 hours or more depending on the challenge test performed. When patients were discharged, they were advised to photograph any late reactions and/or to visit their health center. The test result was considered positive when hives or angioedema with onset of itching appeared on the area of skin exposed. The protocols used for challenge tests were based on those proposed by international guidelines for IU with some modifications,[2,16] as follows.

Ice cube test. The test was performed by inserting an ice cube in a plastic bag and applying it against the skin of the anterior surface of the forearm for at least 5 minutes and then observing the area for around 10 minutes. In the case of a positive result, the exposure time was reduced by 1-minute intervals to find the threshold at which the reaction was triggered. In the case of a negative result, the test was repeated by increasing the time up to 10 minutes. Each exposure was at a different skin site.

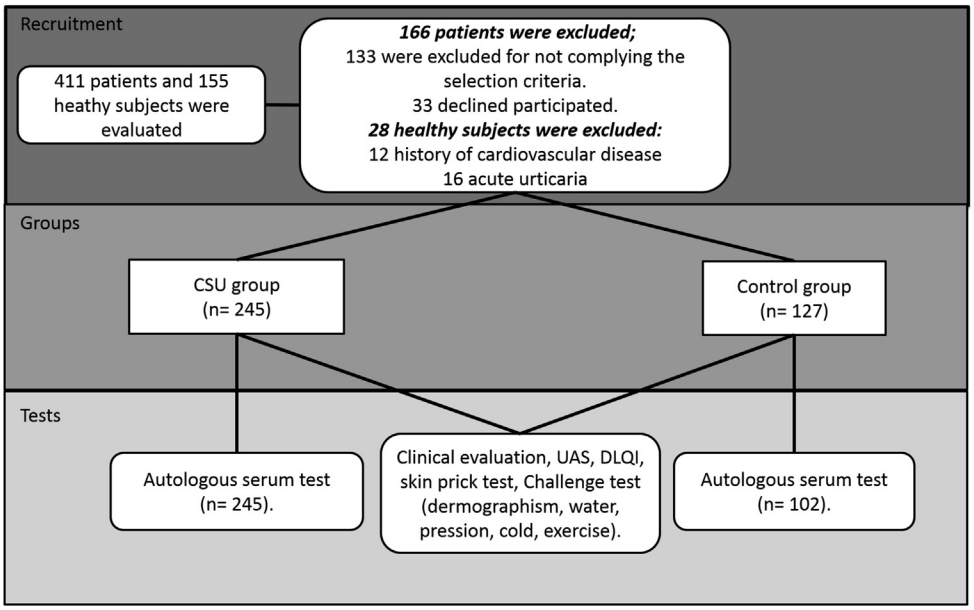

FIGURE 1. Study design.

Water test. The water test was performed by immersion of the patient's forearm in a water bath (20°C-24°C) for a period of 30 minutes. Readings were taken after 10 and 30 minutes of exposure. Additional readings were taken if delayed reactions were suspected.

Pressure test. A bag equal to 10% of the patient's body weight (with a minimum of 7 kg) was applied over the patient's shoulder for 15 minutes. Readings were taken after 20 minutes and 6 and 24 hours.

Dermographism test. The dermographism test was performed in triplicate by drawing a line on the anterior surface of the forearm using a narrow object (a rigid plastic rod). After 10 minutes, the formation of wheals and pruritus was evaluated. Elevation of the skin without itching was considered asymptomatic dermographism and was not considered positive for dermographism urticaria. Additional readings were taken if delayed reactions were suspected. When we started the study, the dermographometer and Fric test were not available; therefore, we used a rigid plastic bar. During the follow-up period, we received a Fric test and began to use it. We saw the benefits of using the Fric test over the narrow object in that we were able to apply measurable degrees of pressure. However, for purposes of defining whether the result for dermographism was positive or not, the Fric test and the narrow object were highly correlated (almost 100%). Furthermore, taking into consideration that not all patients underwent the Fric test (ie, they were tested with the narrow object), we decided to report a positive test result as that obtained with the narrow object.

Exercise test. We used the exercise test to evaluate cholinergic urticaria under the supervision of a specialist in cardiovascular recovery, who monitored the patient's cardiac function. A treadmill was used until the patient began to sweat, at which point the patient continued running for 15 minutes. Readings were taken at 10 and 30 minutes and 2 hours after finishing the test. Vital signs were recorded before and after the challenge test.

A physical challenge test was performed in patients with a strong suspicion of exacerbation with other triggers such as high temperature.

Ethical considerations

This study was approved by the Ethics Committee of IPS Universitaria and the University of Antioquia. All participants (or their legal representative) were asked to sign an informed consent document.

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 21.0 program (IBM Corp, Armonk, New York). The mean and SDs were reported for descriptive variables. Differences between proportions were analyzed using the Pearson chi-square test. Correlations were assessed with the Pearson coefficient (R) when it was necessary to compare nominal variables.

Univariate and multivariate binary analysis based on logistic regression were performed for categorical variables to assess the relationship between exposure and outcome (eg, presence or absence of different types of urticaria). The exposure variables (or predictive variables) included were city of residence, age, sex, age of onset of symptoms, and severity. Depending on their relevance, these variables were also included as covariates in the multivariate analysis. The crude risk (odds ratio [OR]) and adjusted risk (adjusted OR) were reported with a 95% CI.

Given the sample size of previous studies evaluating the presence of IU, we considered that a sample of at least 200 patients would be adequate to ensure a power of 90% and an alpha error of 0.05 for the primary outcome measure (ie, the frequency of IU in patients with chronic urticaria). A P value of less than .05 was considered statistically significant.

RESULTS

General characteristics

Of 411 patients with CSU and 155 healthy subjects who agreed to participate in this study, 245 and 127, respectively, were included (Table I), with a female predominance in both groups (61% and 62%). In terms of origin, 251 participants were from Medellín and 121 were from Bogotá. Asthma was

TABLE I. Baseline characteristics

Variables	CSU group* (n = 245)	CSU Medellin (n = 174)	CSU Bogotá (n = 71)	Control group (n = 127)
Age (y)	28 (14-50)	28 (14-50)	28 (14-48)	27 (15-55)
Age of onset (y)	25 (4-49)	25 (6-49)	25 (4-47)	NA
Sex: female, n (%)	150 (61)	102 (58)	48 (67)	79 (62)
Medellín/Bogotá	174/71	174	71	77/50
Atopy, n (%)	105 (42)	70 (40)	35 (49)	37 (29)
Asthma, n (%)	36 (14)	23 (13)	13 (18)	5 (3)
Rhinitis, n (%)	105 (42)	76 (43)	29 (40)	50 (39)
DLQI score, mean ± SD	15 ± 3	15 ± 3	16 ± 3	NA
UAS, mean ± SD	3 ± 1	3 ± 1	3 ± 1	NA

NA, Not applicable.
*The CSU group includes patients from Medellín and Bogotá.

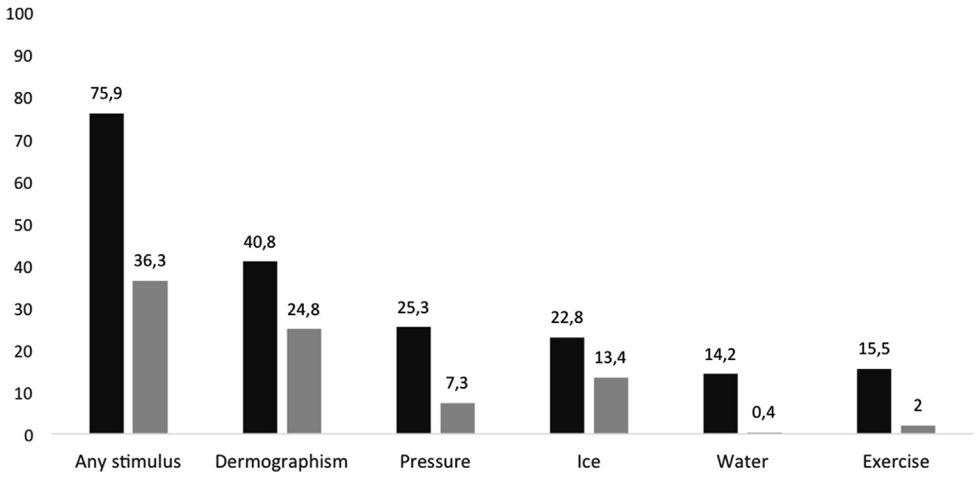

FIGURE 2. Prevalence of IU according to self-report (black columns) and challenge test (gray columns).

significantly more frequent in patients with CSU than in the control group ($P < .05$). No significant sex or age differences were observed between the CSU group and the control group (Table I). The median duration of symptoms was 4 years (mode, 1 year; minimum, 0 year; maximum, 23 years).

IU by self-report and challenge tests

Of the 245 patients, 186 (75%) suspected at least 1 trigger from among the physical stimuli studied, and of these, 77 (41%) identified at least 2 different triggers. The most common self-reported triggers were friction (40%) and pressure (25%). Eighty-nine of 245 patients (36.3%) had a positive challenge test result (Figure 2). The most frequent positive test results were for symptomatic dermographism (24.8%), followed by cold (13.4%), pressure (7.3%), exercise (2%), and water (0.4%). Twenty-nine patients with CSU (11.8%) had at least 2 positive challenge test results (Figure 3). With respect to self-reporting, 17 of the 18 patients with a positive pressure test result (94%) had self-reported ($P = .001$); in the case of friction, 45 of 61 patients with a positive result (73%) had self-reported ($P = .04$), and in the case of cold, 28 of 33 with a positive result (84%) had self-reported ($P = .001$). However, more patients had self-reported their trigger and then had a negative challenge test result (Table II). Eleven patients who had not self-reported any stimulus had a positive result in 1 of the challenge tests. They all had positive results for the dermographism test, except for 1 who was positive for pressure.

The frequency of positive challenge results in the control group was 5.5% (n = 7); 3.9% of patients tested had a positive result to the dermographism test, and 1 patient had pruritus, which reoccurred on retesting. One control subject (0.7%) had a positive result for the ice cube test and another for the exercise test; however, repeating the tests revealed negative results.

A physical challenge test was performed in 12 patients with a strong suspicion of exacerbation with triggers such as heat or sun exposure. None of the results was positive (data not shown).

All symptoms during the challenge test were mild and disappeared during follow-up, except for 2 patients, who required adrenaline. Self-injectable adrenaline was recommended depending on the clinical history in patients with a history of anaphylaxis, tongue angioedema, or severe symptoms during the challenge test.

UAS and DLQI

According to the DLQI and UAS, there were no significant differences between patients with a positive or negative challenge test result or who had self-reported triggers, although the UAS tended to be higher among patients with positive results for self-reporting (Table III).

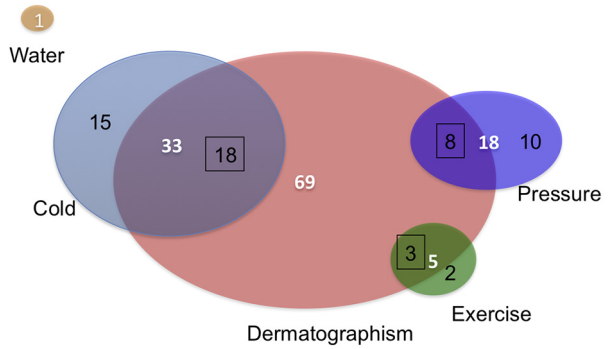

FIGURE 3. A total of 89 patients had at least 1 positive challenge test result. White numbers: Total number of patients positive for each challenge test (dermographism, n = 69; cold, n = 33; pressure, n = 18; exercise, n = 5; and water, n = 1). Numbers in boxes: Patient with at least 2 triggers for IU. Black numbers: Patients with only 1 IU. Red circle: Dermographism. Blue circle: Cold. Purple circle: Pressure. Green circle: Exercise. Orange circle: Water.

IgE sensitization and self-reactivity

Of the 245 patients, 144 (58%) associated symptoms with at least 1 food. Thirteen patients had a positive skin prick test result for food allergens (4 to milk, 3 to egg, 1 to pork, and 5 to fruit and vegetables). Only 2 of these 13 patients had a positive reaction to the food that they reported as a possible trigger of chronic urticaria. Clinical relevance was not clear in the remaining 11 patients.

All the patients in the CSU group and 102 subjects in the control group underwent the autologous serum and plasma skin tests to evaluate self-reactivity. In the CSU group, 93 patients were positive to serum or plasma (62 for both, 15 for serum only, and 16 for plasma only); in the control group, results were positive for 29 (19 for both, 4 for serum only, and 6 for plasma only). Given the close association between serum and plasma in both groups, we considered that a positive result to either indicated self-reactivity. When the CSU and control groups were compared, the frequency of sensitization to mites (42% vs 29%) and self-reactivity (39% vs 28%) were higher. Both variables conferred a significant risk of CSU (atopy: OR, 1.823 [95% CI, 1.153-2.88; $P = .01$] and self-reactivity: OR, 1.650 [95% CI, 1-2.72; $P = .049$]) (Table IV). These risks persisted after adjusting for the patient's age, age at onset of symptoms, sex, and city of residence. No significant covariance was observed between these 2 variables. We observed no association between the presence of atopy or self-reactivity according to the presence of IU, severity of symptoms (UAS), or impact on quality of life (DLQI).

Environmental factors and IU

When comparing patients with IU according to their place of residence, we found an increased risk of symptomatic dermographism, with an OR of 2.1 (95% CI, 1-4.4; $P = .03$), and cold urticaria, with an OR of 3.3 (95% CI, 1.1-9.8; $P = .02$) in patients with CSU from Medellín compared with those from Bogotá (Figure 4). No significant differences were found for other types of IU.

DISCUSSION

Most patients with CSU frequently associated exacerbations with several triggers.[5] Nevertheless, the suspected trigger does not always induce symptoms, with the result that patients often subject themselves to unnecessary restrictions and changes in lifestyle. We observed a wide disparity between self-reporting and physical challenge test results among patients with CSU: according to self-reported data, 75.9% of patients with CSU had IU, although when the challenge test was performed, only 36.3% were positive. Recognizing the authentic trigger is critical, considering that avoidance measures can be quite difficult to ensure and even bothersome (eg, avoiding swimming pools, specific foods or cold drinks, and exercise). One explanation for the discrepancy between self-reported data and the challenge test result is the lack of sensitivity of the physical test, although we believe that the discrepancy is more likely because patients with CSU are seeking a culprit for their disease and identify many triggers with no clear evidence. This also explains why a significant number of patients who associated exacerbation of symptoms with food had negative skin test results and then reported during the physical examination that the symptoms are not always reproduced when they eat the culprit food or were exposed to the physical trigger. Patients probably overestimate the role of the trigger, because urticaria can occur spontaneously and the patient tends to associate exacerbations with the activity performed immediately before onset. Physical challenge tests can identify the actual triggers that cause the reaction, thus enabling more precise recommendations to be made and the impact on quality of life of the affected individual to be reduced. The prevalence of IU varies widely across studies. We found the frequency of IU to be higher among patients with CSU than that reported in the meta-analysis of Trevisonno et al[5] (36.3% vs 13%, respectively). Our findings for patients with self-reported IU and a positive physical test result (41.9%; n = 186) were lower than those of Komarow et al[7] (73%; n = 76). This discrepancy could be explained by selection bias and the instruments used for assessment. Nevertheless, taking into account that the methodology used by Komarow et al was similar to that used by our group, other factors such as sociodemographic characteristics have to be taken into account as a possible explanation for the discrepancies observed.

As has been reported elsewhere, we observed that symptomatic dermographism was the most frequent type of IU among patients with CSU (both self-reported and positive challenge test results). Given that asymptomatic dermographism is present in a high proportion of patients without urticaria, it could be interesting to evaluate in future studies whether asymptomatic dermographism could be a risk factor for symptomatic dermographism. Pressure was the second most frequently reported physical trigger, although very few challenge results were positive. Nevertheless, most patients with self-reported pressure urticaria had positive results in the friction test; therefore, we think that the high prevalence of self-reported pressure urticaria could be explained by the difficulty in differentiating between the 2 stimuli when no provocation test is performed. Cold was the third most frequently reported trigger, with a high correlation between self-reporting and a positive ice cube test result, maybe because this stimulus is easier for the patient to differentiate than the others. Although about half of most reported cases of physical urticaria were confirmed by objective testing, only 1 of 35 patients

TABLE II. The relationship between challenge testing and self-reporting in the CSU group (n = 245)

Type of IU	Positive challenge	Self-report	+/+	+/−	−/+	−/−	*P*
Any	89 (36.3%)	186 (75.9%)	78	11	108	48	>.05
Dermographism	61 (24.8%)	100 (40.8%)	45	16	55	129	.04
Pressure	18 (7.3%)	62 (25.3%)	17	1	45	182	.001
Cold	33 (13.4%)	56 (22.8%)	28	5	28	184	.001
Water	1 (0.4%)	35 (14.2%)	1	0	34	210	>.05
Exercise/heat	5 (2%)	38 (15.5%)	2	3	36	204	>.05

+/+, Positive challenge test and positive self-report; +/−, positive challenge test and negative self-report; −/+; negative challenge test and positive self-report; −/− negative challenge test and negative self-report.

TABLE III. Comparison of UAS and DLQI scores between patients with a positive or negative challenge result and self-report

		Self-report		Challenge test	
Type of IU	Response	DLQI score	UAS	DLQI score	UAS
Any	Yes	16.0	3.5	15.8	3.4
	No	15.3	3.3	15.9	3.5
Symptomatic dermographism	Yes	16.3	3.6	15.9	3.5
	No	15.5	3.4	15.8	3.4
Pressure	Yes	16.2	3.7	15.4	3.5
	No	15.7	3.4	15.9	3.5
Cold	Yes	16.3	3.6	16.1	3.5
	No	15.7	3.4	15.8	3.5
Water	Yes	15.5	3.4	15.0	4.0
	No	15.9	3.5	15.8	3.5
Exercise/heat	Yes	14.6	3.1	14.8	2.6
	No	16.1	3.5	15.9	3.5

DLQI, Dermatology Quality of Life Index.

TABLE IV. Evaluation of atopy and self-reactivity as risk factors for urticaria

Risk factors	Risk-adjusted OR (95% CI)	*P*	Risk-adjusted OR (95% CI)	*P*
Atopy	1.823 (1.153-2.88)	.01	1.923 (1.253-2.78)	.01
Self-reactivity	1.650 (1-2.72)	.04	1.550 (1-2.32)	.05

$P < .05$ was considered statistically significant.

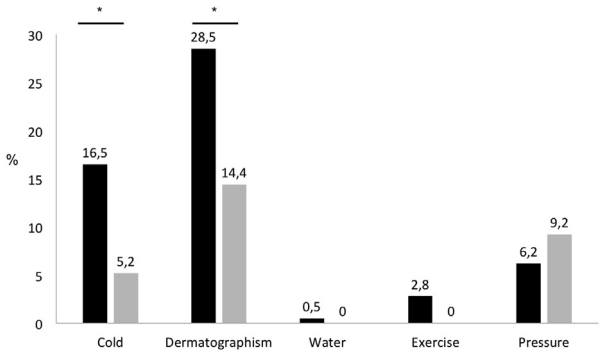

FIGURE 4. Frequency of inducible urticaria between patients with CSU from Medellín (black) and Bogotá (gray) (*$P < .05$).

reporting water as a trigger had aquagenic urticaria, with a negative result for the other tests. Such disparate results could have been due to confusion with other physical triggers, such as cold urticaria. Nevertheless, only 13 of the 35 patients had a positive result for at least 1 physical test and only 5 for the ice cube test. A similar result was found for exercise urticaria, with self-reporting in 38 patients and a positive test result in only 5.

Consistent with Komarow et al,[7] we recorded no fatalities, thus illustrating the low risk of the tests, although 1 patient experienced an episode of anaphylaxis during the exercise challenge test. We recommend that this test be performed only in health centers with resuscitation equipment and trained personnel. The patient had not previously experienced an episode of anaphylaxis, although after the challenge test he reported mild nasal and cutaneous symptoms with high-performance exercise. We also performed a physical challenge test in a group of healthy controls, taking into consideration that, to our knowledge, previous studies had not assessed the frequency of false positives arising from these tests. Because we found a low rate of false positives in the challenge test, we believe this approach is very specific.

We observed similar DLQI scores and UAS in patients with positive and negative challenge test results, although when we inquired about the restrictive measures taken by patients who self-reported, we noted that many restrictions are self-imposed by patients and limited their daily activities (eg, avoiding strong rubbing, tight clothing, and pressing hard with their hands), thus affecting their quality of life in a way that is not measured in the DLQI domains. Therefore, it is necessary to identify the trigger in order to be able to remove these self-imposed restrictions. We did not observe differences in severity according to the UAS between patients with CSU and those with IU. Perhaps severity would have differed significantly between the groups if a more sensitive test such as UAS7 had been used.[3]

Although urticaria is mediated mainly by histamine and mast cells, the underlying mechanisms are not clear. We found that atopy and self-reactivity were independent risk factors for CSU. In some studies, IgE and its high-affinity receptor have been identified as proteins that are recognized by the autoantibodies IgG and IgM, suggesting self-reactivity as a possible pathogenic mechanism. This observation could also suggest that the high IgE levels observed in atopic diseases could act as a potential risk factor leading IgE to be recognized by autoantibodies. Our results support a potential role for atopy and self-reactivity in CSU, although we found that atopy and self-reactivity had low covariance, suggesting possible independent pathophysiological mechanisms, as proposed for other mediators.[17-19]

As stated above, the discrepancy between study results could be explained, at least in part, by differences in sociodemographic characteristics between populations. The populations of Medellín and Bogotá share several sociodemographic factors: both are located in the tropics, the fact that the inhabitants' ancestors are similar means that their genetic background differs little, and both cities share many cultural customs.[10,17] Nevertheless, there are pronounced geographical differences between the cities: Medellín is located at less than 1500 meters above sea level with an average temperature of 22°C (72°F); Bogotá is located at 2630 meters above sea level, with an average temperature of 14°C (58°F). We assessed whether geographical conditions were risk factors for IU and found that the prevalence of dermographism urticaria and cold urticaria was higher in patients located in Medellín. Although we cannot ensure that temperature and altitude were the only factors that explained these differences, we hypothesize that constant exposure to cold environments protects against cold urticaria, probably through a mechanism of desensitization arising from continuous exposure to low temperatures throughout the year in Bogotá. In the case of symptomatic dermographism, peripheral vasoconstriction resulting from the cold temperature could diminish extravasation of the inflammatory mediators necessary for the onset of symptoms. However, multicenter studies to confirm and clarify the influence of these factors are necessary. We found that demographic characteristics did not affect our results, although we cannot rule out the possibility that geographic variables other than altitude and temperature could have some impact.

In conclusion, we found that dermographism and pressure urticaria were common comorbidities in patients with CSU. Therefore, recognition of both conditions by examination of the clinical history and demonstration through specific challenge tests enables us to establish appropriate individualized avoidance measures and thus prevent unnecessary restrictions. Factors such as atopy and self-reactivity seem to play an important role in CSU, and specific geographical characteristics seem to influence the frequency of some types of IU. These findings highlight the need for further studies in different populations to confirm and elucidate other factors that contribute to the development of these disorders.

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