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ORIGINAL RESEARCH

Urticaria Voices: Real-World Experience of Patients Living with Chronic Spontaneous Urticaria

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ABSTRACT

***Introduction*:** The impact of chronic spontaneous urticaria (CSU) on patients' health-related quality of life (HRQoL) is well documented. However, considerable gaps remain in understanding the experience, perception and needs of patients with CSU. In this study, we investigate the perspective of patients with CSU about the disease journey, treatment and management of the condition as well as the physical and psychosocial impact of the disease.

***Methods*:** A multinational, cross-sectional online survey was completed by patients with chronic urticaria (CU) and physicians treating CU. This analysis focuses on data from the patients with CSU. The patient survey included customized questions and a validated patient-reported outcomes measure, the Urticaria Control Test (UCT).

***Results*:** A total of 582 patients with CSU (62% women; mean [standard deviation, SD] age: 42.2 [11.9] years) completed the online survey. Patients reported a mean (SD) diagnostic delay of 2 (5.4) years and saw 6.1 (8.9) physicians. The majority (79%) of patients were on antihistamines, of which 84% were inadequately controlled (UCT score of < 12) and reported a

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significantly higher negative impact of CSU on the HRQoL domains than adequately controlled patients, with the highest impact on mental and emotional well-being and social life and intimate relationships. More than half (55%) of the patients experienced angioedema with a mean (SD) of 7.7 (14.0) episodes per year. In addition, sleeping problems (62%), pain (55%) and fatigue (49%) were frequently reported physical symptoms during an exacerbation.

***Conclusion*:** Patients with CSU experience substantial burden due to delayed diagnosis, insufficient symptom control (despite treatment) as well as mental and emotional well-being and social impact, particularly when uncontrolled. Early diagnosis and patient-centered approaches to symptom management and disease control should be prioritized to minimize the negative impact of CSU on patients' life.

Keywords: Antihistamines; Angioedema; Chronic spontaneous urticaria; Disease/CU/symptom control; Physical symptoms; Psychological impact; Quality of life; Real world experience; Urticaria voices

Key Summary Points

Why carry out this study?

Inadequately controlled patients with chronic spontaneous urticaria (CSU) experience a significant negative impact on health-related quality of life, leading to a substantial disease burden.

This study uncovers previously unexplored facets of patients' experiences on living with CSU, shining a spotlight on the comprehensive impact of the disease, including physical symptom characteristics, psychosocial burdens and healthcare gaps.

What was learned from the study?

This research reveals the substantial burden caused by delayed diagnosis, inadequate symptom control and impacts on the physical, emotional and social aspects of patients' lives, reinforcing the importance of holistic and multidisciplinary treatment approaches.

This study underscores the critical need for timely diagnosis and adoption of patient-centered care practices to effectively reduce the negative effects of CSU on patients' health and well-being.

INTRODUCTION

Chronic urticaria (CU) is a frequent, mast cell-driven disease (lasting for > 6 weeks), causing swollen, itchy and sometimes painful raised areas or "wheals" ("hives") on the skin and is often associated with angioedema [1]. Angioedema in CU is characterized by swelling of deep layers of the skin, often accompanied by erythema, intense itching or burning; usually, it resolves within 72 h [1]. CU is classified as chronic spontaneous urticaria (CSU), in which no external trigger can be identified, and chronic inducible urticaria (CIndU), in which an identifiable trigger is documented [2]. The substantial physical burden of CSU significantly affects

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a patient's daily life, including emotional and psychological well-being, sleep and daily activities [3].

The latest international EAACI/GA^{2}LEN/EuroGuiDerm/APAAACI guideline on the treatment of urticaria recommends first-line second-generation H1-antihistamines (H1-AHs) at the licensed dose or increased dose and add-on omalizumab if control is not achieved [1]. The guideline also emphasizes the principles of stepping up or stepping down in the treatment algorithm according to the course of the disease. Although a clear CU guideline on diagnosis and treatment is in place, real-world studies [3–6] have shown that a significant number of patients have symptoms that are not adequately controlled despite treatment.

Several studies have also reported the negative impact of CSU on patients' health-related quality of life (HRQoL) and emotional well-being [7, 8]. However, these studies have often focused on clinical outcomes and typical patient-reported outcomes (PROs). These tools, although valuable, often do not fully capture the multifaceted burden experienced by patients with CSU and might not comprehensively reflect patients' experiences, perceptions and the full impact of the disease on their daily lives [3, 9].

This international study aimed to fill these knowledge gaps by investigating the experiences and perceptions of patients with CSU regarding their disease journey, treatment and management of CSU. We employed a methodology involving both patients and clinicians, using customized questions designed to provide deeper insights into the physical and psychosocial impact of the disease, surpassing the scope of traditional PROs. This study specifically aims to explore additional physical symptoms beyond itch and hives and the potential stigma associated with CSU from the patients' perspective, thereby further contributing to the current understanding of the disease.

METHODS

Study Design

Urticaria Voices was a non-interventional, cross-sectional study of patients with CU and physicians treating CU. Both patients and physicians self-completed online surveys (see "Study design" in the Online Repository).

Eligible patients with CU in the USA, Canada, UK, Germany, France, Italy and Japan completed a 40-min online survey between February 22, 2022, and September 15, 2022.

All respondents could complete the online surveys from any device (computer, tablet or smartphone).

Participants

Individuals had to be > 18 years old at the time of data collection, to have a self-reported, clinician-provided CSU and/or CIndU diagnosis, at the time of the survey receiving a physician-prescribed medical treatment for their chronic urticaria, to not have participated in a clinical trial for CU and not be employed by a pharmaceutical or market research company.

Patients were recruited from a general population panel of individuals who had previously consented to be contacted regularly for primary research studies owned and operated by Ipsos SA and its global partner. A random sampling from online panels of the general population was enriched with snowball sampling with the help of patient advocacy groups (PAGs), where applicable. Selected PAGs extended invitations to their patient members to complete the patient survey.

Variables

Variables considered during the analysis (Table 1) were selected from study-specific questions on experiences and perceptions of disease journey, treatment and burden of the disease according to patients with CSU. Patients were asked to rate the negative impact of CSU on their lives using a 10-point Likert scale ranging

Table 1 Patient study variables

Domain	Variable
Health history	CSU or CIndU diagnosis
	Disease characteristics (e.g., angioedema, number of angioedema episodes, outbreak symptoms, pain location, pain type)
	Disease history (e.g., time since first onset, time since diagnosis, number of specialists seen, number of main doctor switches, reasons for doctor switch)
Treatment patterns/disease control	Treatments used (e.g., currently, previously), level of symptom control, number of AH switches, number of AH up dosing, improvement from AH updosing, side effects from AH updosing
Life domain	Experience of living with CU (e.g., overall impact on daily life, main domain / aspects of life affected, ability to reach full potential, negative experiences)

AH antihistamine; *CIndU* chronic inducible urticaria; *CSU* chronic spontaneous urticaria; *CU* chronic urticaria

from 1 (not at all negatively impacted) to 10 (extremely negatively impacted). The Likert scale is a widely recognized method for assessing subjective experiences [10], and we customized it to suit it to our study objectives.

The level of CU disease control was assessed using a validated PRO measure (PROM), namely the Urticaria Control Test (UCT) [11]. The UCT measures the level of CU disease control over the last 4 weeks and contains four questions covering physical symptoms (itch, hives, swelling), quality of life (QoL) impact, frequency of treatment inadequacy and overall CU control. Each question is assigned a score from 0 to 4, with higher scores representing improved disease control. A UCT score of <12 indicates poorly or inadequately controlled CSU.

The collected patient demographic information included age, country, gender, highest level of education, current occupation status and current relationship status.

Data Sources

The data sources for patient variables were self-administered online surveys. Answers were based on respondents' estimations, perceptions and overall experiences (not medical records or secondary data).

Study Size

Precision-based sample size calculation was used to calculate the minimum needed sample size of patients and physicians for the overall study. For the confidence level of 95%, which is standard in the scientific community, the minimum sample size to reach a desirable precision of 5% is 384 respondents per target group (patients and physicians). Details on the sample size calculation are provided in the electronic supplementary material.

Recruitment and Handling of Personal Data

Informed opt-in consent was sought from respondents before fieldwork. Regardless of the sample origin, all participants electronically confirmed the read receipt of their informed consent forms before proceeding with the survey. This study was conducted in accordance with the ethical principles laid down in the Declaration of Helsinki.

Respondents were informed that they could withdraw from participation at any time, including after survey completion. Following survey completion, respondents recruited by Ipsos were compensated according to fair market values. Patients recruited by PAGs were not compensated.

This study was conducted in accordance with legal and regulatory requirements and fulfilled the criteria of a "European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCePP) study" and followed the "ENCePP Code of Conduct." An exemption from ongoing oversight was obtained from the Pearl Institutional Review Board (IRB), who reviewed and granted international approval of an exemption.

Data collected during the survey were used and stored in accordance with industry regulations and laws governing confidentiality and according to legal, compliance and regulatory requirements covering any research with patients. Respondents were assigned numerical respondent IDs so that answers could not be linked to individual patients. At no point during any of the patient survey was personal information such as name or address captured. All data are reported in aggregate format and all participants retained anonymity.

Analysis

The analysis in this publication was performed on patients diagnosed with CSU. The research objectives were analyzed descriptively. Continuous variables of interest were summarized in terms of means, 95% confidence intervals and standard deviations (SDs). Answers from multiple-choice questions were transformed into binary categorical variables (i.e., yes/no) and reported as percentage of respondents choosing them. Furthermore, a comparison was made between inadequately controlled patients (UCT < 12) and adequately controlled patients (UCT 12–16) to understand the impact of the disease on their HRQoL domains. An independent sample *t*-test was utilized to establish whether the mean difference between these patient groups indicated a statistically significant difference. All statistical analyses reported exact *p* values at an alpha level of 0.05. Where missing values were found in a variable, any corresponding respondents were removed from all pieces of analysis where that variable was used. Sensitivity analysis was not performed.

RESULTS

Demographics and Clinical Profile of the Patients with CSU

A total of 582 patients diagnosed with CSU were included in this analysis, with 212 (35.8%) having concomitant CIndU (Table 2). The mean (SD) age at data collection was 42.2 (11.9) years, and 62% were female. The mean (SD) disease duration was 9.2 (10.3) years and 7.1 (8.5) years since patients were officially diagnosed with CSU. Almost half of the patients (45%) had symptoms for more than a year before receiving the diagnosis and 55% reported angioedema, with a mean (SD) of 7.7 (14.0) episodes per year. Additional country-level data can be found in the electronic supplementary material (Tables S1–S28).

Patient Journey

Patients with CSU reported a mean (SD) of 2 years (5.4) from the time they first started experiencing symptoms to the time of diagnosis. During this period, patients with CSU consulted a mean (SD) of 6.1 (8.9) physicians.

Almost half of the patients with CSU have changed the physician responsible for managing their CSU at least once since the diagnosis. The most frequently reported reasons for switching doctors were the wish to find a more specialized doctor (36%), closely followed by the wish to be considered for a more effective treatment (29%) and/or to maintain CU symptoms fully under control (29%).

In terms of unmet needs, patients placed equal importance on more knowledge of CU among primary care physicians (46%), more knowledge about the underlying causes of CU (45%), better information about available treatments (44%) and better access to specialized doctors (43%) and treatments (42%).

Treatments and Disease Control

At the time of the study, 79% of patients with CSU were treated with various types of antihistamine. Additionally, patients were taking

Table 2 Patient characteristics and demographics

	All CSU (*N* = 582)	**CSU-only (*N* = 370)**	**CSU + CIndU (*N* = 212)**
Age (years), mean (SD)	42.2 (11.9)	43.2 (12.1)	40.4 (11.2)
[95% CI]	[41.2–43.2]	[42.0–44.4]	[38.9–41.9]
Gender, *N* (%)			
Female	362 (62%)	225 (61%)	137 (65%)
Male	220 (38%)	145 (39%)	75 (35%)
Years since onset, mean (SD)	9.2 (10.3)	8.1 (9.8)	11.1 (10.7)
Years since CU diagnosis, mean (SD)	7.1 (8.5)	6.2 (7.9)	8.7 (9.4)
No. of years between onset and diagnosis, mean (SD)	2.0 (5.4)	1.8 (5.3)	2.3 (5.6)
Number of comorbidities, mean (SD)	2.4 (2.7)	1.9 (2.1)	3.3 (3.3)
Adequate control (UCT 12–16), *N* (%)	114 (20%)	89 (24%)	25 (12%)
Inadequate control (UCT < 12), *N* (%)	468 (80%)	281 (76%)	187 (88%)
Current treatments, mean (SD)	2.9 (2.6)	2.4 (2.1)	3.7 (3.1)
Any antihistamines, *N* (%)	460 (79%)	272 (74%)	188 (89%)
Any steroids, *N* (%)	290 (50%)	173 (47%)	117 (55%)
Any biologic, *N* (%)	193 (33%)	106 (29%)	87 (41%)
Exclusively on antihistamines, *N* (%)	138 (24%)	87 (24%)	51 (24%)
Exclusively on steroids, *N* (%)	45 (8%)	37 (10%)	8 (4%)
Exclusively on biologics, *N* (%)	18 (3%)	14 (4%)	4 (2%)
On mixed treatment, *N* (%)	381 (65%)	232 (63%)	149 (70%)
Country, *N* (%)			
USA	152 (26%)	105 (28%)	47 (22%)
Canada	73 (13%)	52 (14%)	21 (9.9%)
UK	87 (15%)	45 (12%)	42 (20%)
Germany	79 (14%)	44 (12%)	35 (17%)
France	86 (15%)	53 (14%)	33 (16%)
Italy	64 (11%)	41 (11%)	23 (11%)
Japan	41 (7%)	30 (8%)	11 (5%)

Patients using any combination of medications, such as antihistamines, steroids and biologics, were categorized as being on mixed treatment

CI confidence interval*; CIndU* chronic inducible urticaria*; CSU* chronic spontaneous urticaria; *CU* chronic urticaria; *SD* standard deviation; *UCT* Urticaria Control Test

concomitant glucocorticoids in different forms: 36% as creams, 24% oral and 13% intravenous forms. Notably, these treatments are not mutually exclusive, and some patients may have been using more than one form of glucocorticoid.

Of the patients with CSU, 80% of patients were inadequately controlled in the last 4 weeks (UCT < 12). Of the patients using any type of AHs as part of their treatment, 84% remained inadequately controlled (UCT < 12), 53% were taking second-generation H1-AHs and 48% were taking first-generation H1-AHs (of which 19% were taking both first and second-generation H1-AH). Additionally, 78% of patients who relied exclusively on antihistamines for managing their condition also remained inadequately controlled. Four out of five patients taking AHs reported being switched to another type of AHs by their physician and over half reported having the dosage of current AHs increased. Three out of four patients who received an increased dosage indicated either no relief (7%) or only partial (68%) improvement in their symptoms.

Burden of CSU

Angioedema Frequency and Impact

Over half of the patients with CSU (55%) reported having angioedema at one point in their life. Among those patients who had angioedema, two in five (43%) reported experiencing angioedema in the past 12 months despite treatment, with a mean (SD) of 7.7 (14.0) angioedema episodes, with 57% experiencing pain at the angioedema site.

Other Physical Symptoms

Physical symptoms beyond itch, hives and angioedema are reported in Fig. 1. Most of the physical symptoms were experienced during an exacerbation. Three out of five patients reported experiencing sleeping problems (62%), and half of the patients reported experiencing pain (55%) and fatigue (49%) during an exacerbation. Among patients who experienced pain, it was most frequently reported to be located at the region of hives (59%), angioedema (34%) and joints (34%). Burning or stinging pain was reported most frequently (70%), followed

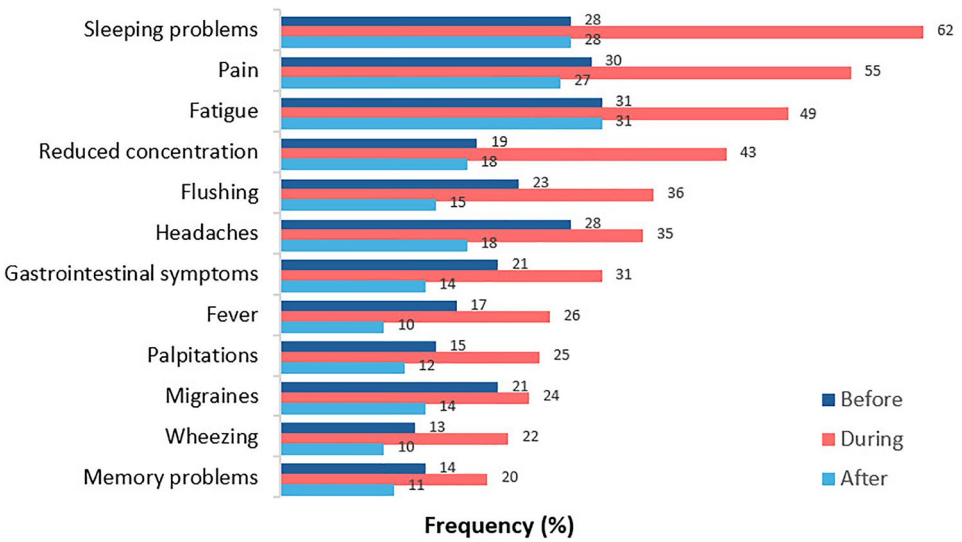

Fig. 1 Physical symptoms of patients with CSU other than itch and hives before, during and after an exacerbation. *CSU* chronic spontaneous urticaria. The question in the patient survey used the patient-friendly word "outbreak."

by aching/swelling (61%) and soreness after scratching the skin (57%).

Emotional, Cognitive and Social Burden of CSU

Patients were asked to rate the overall impact of CSU on their lives and impact of CSU on HRQoL domains, on a scale from 1 to 10, where 1 represented "not at all negatively impacted" and 10 denoted "extremely negatively impacted." Patients reported an overall moderately negative impact (mean [SD] score, 6.6 [2.2]) of CSU on their lives. Eighty percent of the patients with CSU were inadequately controlled (UCT < 12; Table 2). Inadequately controlled patients reported significantly ($p < 0.05$) higher overall negative impact (mean [SD] score, 7.0 [1.9]) across all HRQoL domains (mental and emotional well-being: 6.3 [2.6]; social life and intimate relationships: 5.8 [2.7]; activities of daily living: 5.6 [2.8]; financial: 5.0 [2.8]) than

Table 3 Stigma associated with CSU among patients

	Patients with CSU ($N = 582$) N (%)
Being asked if I'm contagious	192 (33%)
Being stared at in public	192 (33%)
People refusing to shake my hand or touch me	103 (18%)
Being made the center of jokes	88 (15%)
Bullying	68 (12%)
Humiliation in public	71 (12%)
Public discrimination	57 (10%)
None of the above	223 (38%)

CSU chronic spontaneous urticaria

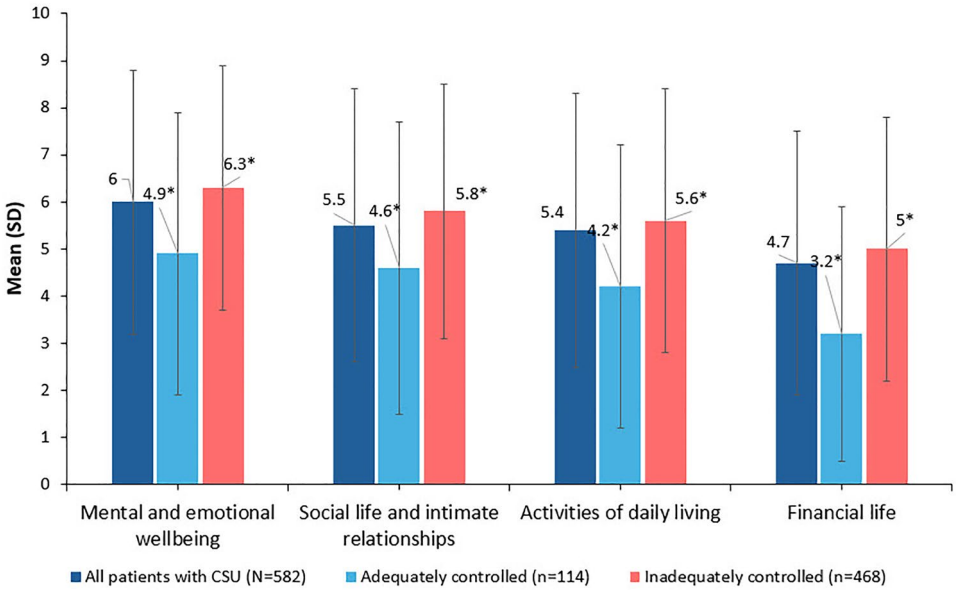

Fig. 2 Emotional, cognitive and social burden of CSU. *CSU* chronic spontaneous urticaria; *SD* standard deviation; *UCT* Urticaria Control Test. 1. The negative impact was assessed using a 10-point Likert scale: "Not at all negatively impacted" (1) to "Extremely negatively impacted" (10). 2. Patients with a UCT score of ≥ 12 are identified as adequately controlled patients with CSU; patients with a UCT score of < 12 are identified as inadequately controlled patients with CSU. 3. *$p < 0.001$; statistically significant differences between adequately and inadequately controlled patients were assessed with independent samples *t*-tests assuming unequal variances due to the different sample sizes

adequately controlled patients (UCT 12–16; overall negative impact: 5.1 [2.4]; mental and emotional well-being: 4.9 [3.0]; social life and intimate relationships: 4.6 [3.1]; activities of daily living: 4.2 [3.0]; financial: 3.2 [2.7]; Fig. 2).

Patients with partners had a greater impact on family life (mean [SD] score, 5.1 [2.8]) versus those without (mean [SD] score, 4.2 [3.0]). Similarly, the impact on professional life was more prominent in patients with university education (mean [SD] score, 5.0 [2.9]) versus those without (mean [SD] score, 4.3 [3.1]), respectively.

Patients indicated a mean (SD) impact of CSU on their ability to reach full life potential of 7.2 (2.2), on a scale from 1 to 10, where 1 represented "not able at all to reach full potential," and 10 represented "completely able to reach full potential."

Stigma and Discrimination

Living with CSU brought some form of stigma and discrimination in 63% of patients (Table 3). A third of patients reported being stared at in public (33%) or asked if they are contagious (33%). One in six patients (18%) reported that some people refuse to shake their hand or touch them, and one in seven (15%) said they are made the center of jokes. A small proportion of patients reported being bullied (12%), humiliated (12%) or publicly discriminated (10%).

DISCUSSION

This international study of patients with CSU reveals new aspects of patients experience on living with CSU and its consequences as well as reasserts the burden of the disease. This study highlights key challenges for patients with CSU, including diagnostic delays and treatment challenges, inadequate disease control, physical symptoms, HRQoL, emotional, social, and economic burden and healthcare gaps.

Delayed Diagnosis and Treatment-Related Challenges

Patients with CSU continue to experience a delay in diagnosis as well as the need to see multiple doctors during this timeframe [3]. In our study, an average diagnostic delay of 2 years aligns with the findings reported in prior studies, which indicate an average delay of approximately 2–4 years from symptom onset to diagnosis [12]. Almost half of the patients switched doctors after the diagnosis, aiming to find a more specialized doctor, be considered for a more effective treatment and/or keep their symptoms fully under control. The results were consistent with those of previous studies [13, 14] that have reported these gaps in patient management. In an Italian study of 190 patients, 75% visited three or more physicians before receiving a CSU diagnosis or having an appropriate treatment prescribed [14]. In-line with the reasons for switching doctors, patients expressed the need for more knowledge about CU among primary care physicians and better access to specialized care and treatments [12].

Inadequate Disease Control

At the time of the study, most patients reported inadequate disease control in the last 4 weeks as assessed with the UCT. These findings are in line with those of other real-world studies [3–6] on patients with CSU. The lack of symptom control (UCT < 12) was particularly prominent in patients taking AHs, despite attempts to optimize treatment by switching and updosing AH medications. In the group of patients who received an increased dosage, three of four experienced either no alleviation or only partial relief of their symptoms. Additionally, a systematic review by Mitchell et al. [15] highlighted that despite current guidelines recommending increased dosages of nonsedating AHs for nonresponders, high-quality data to support the efficacy of this approach are lacking.

Physical Symptoms and HRQoL

Consistent with the findings of previous research by Maurer et al. [3, 16] and Kolkhir et al. [4], the findings from this study indicate the substantial negative impact of CSU on patients' HRQoL. The current study further describes a substantial burden of angioedema, reinforcing the results of earlier research by Sussman et al. [17]. Previous studies [3, 18–20] have indicated that pain, sleep and fatigue are prevalent symptoms negatively impacting the quality of life of patients with CSU. A study by Maurer et al. [3] highlighted the substantial burden of CSU, including disrupted sleep and significant discomfort during exacerbations, with pain being indirectly addressed through related symptoms such as itching and swelling, particularly in the context of angioedema. A study by Sánchez-Díaz et al. [20] emphasized that poor sleep quality is a predictor of impaired quality of life and emotional status in patients with CSU. Mann et al. [19] discussed how sleep disturbances are often underestimated in their impact on patients with urticaria. Another study by Erol et al. [18] demonstrated that fatigue is a common symptom in patients with CSU, particularly among women and those with sleep disturbances. The results of this research corroborate with those of previous findings, indicating that patients with CSU experience sleeping problems, pain and fatigue before, during and after an exacerbation, which strongly points the need for better control in this patient population.

Emotional, Social and Economic Impact

CSU imposes a substantial emotional, social and financial burden on patients, considerably affecting their HRQoL. The findings of this study, consistent with those of prior research [7, 16], suggest that CSU predominantly disrupts mental and emotional well-being. Patients reported an overall negative impact of CSU on their lives, with notably higher scores in the mental and emotional domains, and an impact on the financial domain, especially among those with inadequately controlled disease. The negative impact on professional and academic pursuits were most evident in patients with a university degree, and familial relationships were more impacted among those in a partnership. However, other research [21, 22] has shown that greater disease severity is linked to substantial impairment in work productivity and social engagement regardless of educational and relational factors.

A previous study by Wiis et al. [23] revealed that 57.3% of patients with CSU experienced stigmatization. The findings of this study are consistent with those of Wiis et al., with over half of the patients reported experiencing stigma and discrimination, including being stared at in public, asked if they are contagious, refused handshakes or touches, and being made the center of jokes. These findings underpin the importance of managing the emotional aspects of CSU, which is crucial for improving overall HRQoL.

The chronic and unpredictable nature of CSU substantially affects work productivity, incurs considerable direct and indirect costs and contributes to the overall economic burden experienced by patients [3]. Studies conducted in the EU5, USA and Brazil demonstrated that patients with CSU report higher overall work impairment than the general population [24–26]. In this study, patients reported considerable burden due to their CSU, especially during episodes of disease exacerbations, with 62% of patients experiencing sleeping problems, 55% experiencing pain and 49% experiencing fatigue. We also observed that inadequately controlled patients reported a higher impact across all HRQoL domains, including financial strain, with a mean score of 5.0 (2.8) compared to that of 3.2 (2.7) in the adequately controlled patients. These experiences may contribute to the overall impairment in work productivity and financial burden of the disease.

Healthcare Gaps: The findings presented in this study highlight critical gaps in the management and treatment of CSU. First, there are considerable delays in diagnosis, highlighting the need for better education among primary care physicians, a need also confirmed by 46% of the patients in our study. Second, despite guidelines recommending treatment escalation

and aiming for full disease control [1], many patients do not achieve this. In this study, we found that patients often cycle through different AHs, with four of five switching to another AH and over half escalating to a higher dose. This pattern was observed over several years (average diagnosis duration: 2 years), without transitioning to more effective treatments despite ongoing symptoms, and despite recommendations in the guidelines [1]. We also noted relatively high use of first-generation AH, with 48% of patients being prescribed these medications, which are not recommended by the international [1] or Japanese guidelines [27]; however, they are recommended for nighttime use in the US treatment guidelines [28], which may explain some diverse prescribing practices. Guidelines recommend short-term rescue use of systemic glucocorticoids and strongly advise against long-term use due to safety risks and lack of evidence for effectiveness in managing CSU [1]; however, our study found common use of steroids, including creams, both as rescue medication and otherwise [29]. This highlights a gap between guideline recommendations and actual clinical practice, underscoring the need for better adherence to guidelines to improve patient outcomes. Furthermore, guidelines suggest referring patients to specialists, when necessary [1], as many face barriers to accessing specialized care. This is evident from the average of 6.1 times patients had to switch physicians to find appropriate care, indicating significant gaps in the healthcare system.

Exploring global treatment patterns and outcomes within this study's dataset could provide further insights into these gaps and contribute to the development of more effective management strategies for CSU.

While these findings provide valuable insights, it is important to acknowledge certain limitations that may influence the interpretation of the results. Patients with CSU who have limited access to the internet and/or limited digital literacy may not have been reached by the study. This limitation was partially compensated for by employing a random sampling technique, inviting a nationally representative sample of potential patients based on age, gender and region of the respective countries. Reassuringly, despite no age quotas, most patients were in their late 30s and early 40s, which matches the age distribution reported in the literature for CU [30, 31]. While digital literacy among younger populations could be an influential factor, individuals from older age groups who have access to the internet were also included in the survey pool, particularly through the PAGs, to broaden the reach. However, despite these efforts, there remains a possibility of inadequate representation of older individuals or those less familiar with digital tools, which is an inherent limitation of all online surveys. This limitation might affect the generalizability of our findings.

The study's cross-sectional design inherently relies on patients' memory for their medication histories, which could have resulted in recall bias. This was mitigated to a large extent by developing clear and specific survey questions, most of which were focused on the "current status" at the time of survey completion. The pilot phase, consisting of computer-assisted telephone interviews, aimed to refine the survey and reduce ambiguities. Additionally, the customized questions were reviewed by PAGs and medical experts to ensure appropriateness and clarity. Despite these measures, participants may not have remembered their medical information precisely. To further mitigate recall bias, the survey included a variety of single- and multiple-choice questions, rating and ranking questions and open-ended questions. All patients completed validated PROMs, such as the Patient Global Impression of Severity to assess symptom severity in the past 7 days, the UCT to assess the level of control in the past 4 weeks and the Patient Activation Measure-13 to assess the level of knowledge, skills and confidence integral to managing one's own health. These validated measures contributed to minimizing recall bias by providing structured and specific questions to assist participants in accurately recalling their experiences. The study's cross-sectional design, capturing a single point in time, limits its ability to track changes in conditions, treatment efficacy and quality of life over time.

In future research, alternative methods may be considered to reach underrepresented populations, such as combining online surveys with traditional data collection methods (e.g.,

telephone interviews or in-person surveys). This mixed-method approach will further enhance inclusivity and help ensure a diverse and more representative sample.

CONCLUSIONS

Patients with CSU experience a substantial burden due to factors such as delayed diagnosis, insufficient symptom control and emotional and social impact of the disease. Poorly controlled disease can significantly hamper the QoL of patients, encompassing not only physical health but also emotional well-being. To minimize these impacts, healthcare systems should prioritize education, earlier diagnosis and achieving well controlled CSU through clear and structured treatment pathways. Key steps include adherence to guidelines, systematic screening of protocols for early diagnosis, efficient escalation of treatment and referrals to specialists as needed, treatment plans that address both physical and psychosocial symptoms, treating until the disease is gone and comprehensive patient education. A multidisciplinary approach involving dermatologists, allergists and psychologists can further support effective disease management. The findings from this study underscore the necessity for increased awareness and understanding of CSU among both patients and clinicians, which is essential for improving patient care and outcomes. This study adds valuable new evidence to the existing knowledge base, highlighting the importance of integrating the patient voice into clinical care and policy decisions to ensure that their needs are fully addressed.

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Data Availability. The data generated or analyzed during this study are included in this published article/as supplementary information files.

Declarations

Conflict of Interest. Karsten Weller reports grants from Novartis and Takeda outside the

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Ethical Approval. This study was conducted in accordance with the ethical principles laid down in the Declaration of Helsinki. IRB / Ethical approval was sought for this study based on the rationale that while the study includes "living people" who will complete the self-administered quantitative internet-based survey, there will be no articles or substances tested; hence Ipsos and the sponsor do not believe that these "living people" would be classified as "human subjects". An exemption from ongoing oversight was sought after and obtained from an IRB, who reviewed and granted international approval. Informed opt-in consent was sought from respondents before fieldwork. Regardless of the sample origin, all participants electronically confirmed the read receipt of their informed consent forms before proceeding with the survey. Compliance with Novartis and regulatory standards provided assurance that the rights, safety, and well-being of patients participating in non-interventional studies are protected, consistent with the principles that have their origin in the Declaration of Helsinki.

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