Brief report

Disparities in chronic spontaneous urticaria: Eligibility for drug reimbursement associated with clinical outcomes

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Background: Chronic spontaneous urticaria (CSU) is an immunologic condition with an estimated prevalence of 0.1%. For CSU that is poorly controlled despite the use of antihistamines, omalizumab is the only treatment approved and recommended by international guidelines.

Objective: Our aim was to outline the impact of treatment accessibility on CSU outcomes in the real world.

Methods: Serial data on adult patients with CSU receiving care for at least 6 months at a dedicated, immunologist-led urticaria clinic at Grantham Hospital in Hong Kong between 2018 and 2023 were analyzed. Patients' clinicodemographic data, drug eligibility status (eligible for reimbursement or not), treatment step, and disease activity (weekly Urticaria Activity Score [UAS7]) were collected and compared according to drug eligibility status.

Results: This study included 238 patients, 80 (33.6%) of whom were eligible for reimbursement and 158 of whom were not. No significant clinicodemographic differences, including disease activity, were found at baseline. At latest follow-up, significantly more patients in the eligible group were receiving omalizumab (28.7% vs 5.7% [$P < .001$]), which is equivalent to a multivariate odds ratio of 9.35 (95% CI = 3.689-23.703 [$P < .001$]). The discrepancy persisted even in patients with moderate-to-severe CSU whose UAS7 was 16 or higher (40.6% [13 of 32] vs 10.2% [6 of 59]; $P < .001$). In addition, there was significantly less dose reduction (<300 mg every 4 weeks) in the eligible omalizumab users (4.3% vs 44.4% [$P = .015$]). Clinically, significantly greater improvements in UAS7 were reported by the eligible group (median change –8.0 vs –5.0 [$P = .021$]).

Conclusion: Patterns of management varied largely among patients with different drug eligibility statuses and led to disparities in health outcomes. More efforts to secure equitable access to guideline-based CSU care are warranted. (J Allergy Clin Immunol Global 2024;3:100243.)

Key words: *Urticaria, chronic urticaria, CSU, health disparities, equity, biologics*

INTRODUCTION

Chronic spontaneous urticaria (CSU) is a common immunologic disorder affecting 0.5% to 1% of the population.[1] It is associated with a myriad of direct and indirect adverse patient outcomes, from impaired quality of life (QoL) to increased allergy misdiagnosis and mislabeling.[2-4] The therapeutic goal in CSU management is complete disease control, with guidelines recommending stepwise pharmacologic therapy.[5] Although the initial step is regular use of second-generation H_1-antihistamines, followed by doses increasing up to 4-fold, omalizumab (licensed dose 300 mg monthly) is indicated for patients with uncontrolled symptoms despite receiving maximal doses of antihistamines (~20%-50% of all patients with CSU).[4] Primarily to save costs, especially in developing countries, lower doses of omalizumab (doses less than the licensed dose) have been attempted with only variable success.[6]

In Hong Kong, omalizumab remains a self-financed item regardless of disease severity, and patients bear the full treatment costs unless they meet eligibility criteria for reimbursement, such as if they meet the requirements of limited means-tested financial assistance schemes or are eligible civil service persons (civil servants and their families). Unfortunately, patients who are ineligible for reimbursement often cannot afford biologics despite experiencing severe and refractory symptoms. Alternatives such as cyclosporin or other immunosuppressants are often declined because of unfavorable side effect profiles. Even among patients who can financially afford omalizumab, many decide to self-reduce to lower-than-recommended doses owing to financial constraints. Therefore, many patients live with persistently active disease and suboptimal QoL.

Although the impact of accessibility to biologics on disease control has become a major area of research for various diseases such as severe asthma, this topic has seldom been studied in CSU.[7] Therefore, we investigated the health disparities in treatment access (specifically omalizumab) and its impact on CSU outcomes.

We analyzed patients with CSU who attended our dedicated urticaria clinic (a certified GA^{2}LEN UCARE and the only CSU referral center in Hong Kong) at the Hospital Authority Hong Kong West Cluster/The University of Hong Kong between January

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Abbreviations used
CSU: Chronic spontaneous urticaria
QoL: Quality of life
UAS7: Weekly Urticaria Activity Score

2018 and December 2022. All patients met the criteria for CSU, and their pharmacologic treatments were managed as per international recommendations.[5] Only adult patients (those aged >18 years) diagnosed with CSU with a follow-up duration of at least 6 months were recruited. Clinical data, including patient demographics, drug eligibility status (reimbursable vs self-financed treatment), baseline Weekly Urticaria Activity Score (UAS7) during their first clinic visit, treatment step, and UAS7 during their latest follow-up, were retrieved following anonymization. Patients were compared according to drug eligibility status. Chi-square tests and independent *t* tests were used for categoric and continuous comparisons, respectively. Paired *t* tests were used for pre-post analysis. Statistical analysis was performed using IBM SPSS Statistics, version 28.0 (IBM, Armonk, NY). This study was approved by the institutional review board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster.

RESULTS AND DISCUSSION

A total of 238 unique patients were analyzed, with a median follow-up of 1.20 years (range 0.78-2.11 years). All of the patients were Han Chinese. Of these patients, 80 (33.6%) were eligible for drug reimbursement, whereas the remaining 158 were ineligible (ie, self-financed their treatment). There were no significant differences in demographic and clinical characteristics or baseline disease activity (Table I).

At latest follow-up, there were significant differences in treatments between the eligible and ineligible groups (Fig 1), with significantly more patients in the eligible group receiving omalizumab (28.7% vs 5.7% [$P < .001$]). After adjustment for potential confounders, only UAS7 and drug eligibility status were independently associated with omalizumab use, with eligible patients being 9.35 times more likely to receive omalizumab (95% CI = 3.689-23.703 [$P < .001$]; Table II). Among all patients who received omalizumab, significantly fewer eligible patients received omalizumab in a dose less than 300 mg every 4 weeks (4.34% vs 44.4% [$P = .015$]). In a subgroup analysis of patients with moderate-to-severe CSU (UAS7 ≥ 16), eligible patients were significantly more likely to receive omalizumab (40.6% [13 of 32] vs 10.2% [6 of 59]; $P < .001$). Although both groups experienced improvements in disease activity, the eligible group reported significantly greater improvements in UAS7 (median change –8.0 vs –5.0 [$P = .021$]; Fig 2).

To our knowledge, we are the first to report the real-world impact of treatment accessibility on CSU outcomes. The cost-effectiveness of omalizumab has been proved to be favorable compared with that of antihistamines at the maximal dose, especially in terms of productivity and QoL, in multiple populations and studies.[8] In spite of this, many health care systems still do not follow international recommendations and do not reimburse biologics even for patients with uncontrolled symptoms despite maximal dose antihistamines.

TABLE I. Demographic and clinical characteristics of patients with CSU according to drug eligibility status

Characteristic	All patients with CSU (N = 238)	Eligible for reimbursement (n = 80)	Ineligible for reimbursement (n = 158)	*P* value
Demographics				
Female sex, no. (%)	182 (76.5)	62 (77.5)	120 (75.9)	.790
Age of onset (y), median (IQR)	34.6 (19.0, 52.5)	41.0 (19.0, 51.0)	33.0 (18.5, 53.0)	.547
Age at first visit (y), median (IQR)	48.4 (34.7, 57.7)	49.4 (34.6, 57.4)	46.9 (34.8, 58.1)	.828
Delay in diagnosis (y), median (IQR)	3.96 (1.61, 17.93)	4.39 (1.88, 13.31)	3.86 (1.56, 18.67)	.912
Follow-up duration (y), median (IQR)	1.20 (0.78, 2.11)	1.22 (0.76, 2.02)	1.20 (0.78, 2.13)	.936
Comorbidity, no. (%)				
Food allergy	23 (9.7)	8 (10.0)	15 (9.5)	.901
Drug allergy	93 (39.1)	27 (33.8)	66 (41.8)	.231
Autoimmune disorder	37 (15.5)	15 (18.8)	22 (13.9)	.332
CSU characteristic, no. (%)				
Self-reported triggers	59 (24.8)	21 (26.3)	38 (24.1)	.710
History of angioedema	163 (68.5)	55 (68.8)	108 (68.4)	.951
Treatment, no. (%)*				**<.001**
Not taking regular medications	26 (10.9)	9 (11.3)	17 (10.8)	
Step 1	118 (49.6)	35 (43.8)	83 (52.5)	
Step 2	57 (23.9)	13 (16.3)	44 (27.8)	
Step 3	32 (13.4)	23 (28.7)	9 (5.7)	
Step 4	5 (2.1)	0 (0.0)	5 (3.2)	
Use of omalizumab, no. (%)	32 (13.4)	23 (28.7)	9 (5.7)	**<.001**
<300 mg every 4 weeks	5 of 32 (15.6)	1 of 23 (4.3)	4 of 9 (44.4)	**.015**
UAS7, median (IQR)				
Baseline	12.0 (3.0, 28.0)	14.0 (6.0, 28.0)	8.5 (2.0, 28.0)	.112
Change at follow-up	–6.0 (–16.0, 0.0)	–8.0 (–16.5, –3.0)	–5.0 (–16.0, 0.0)	**.021**

Boldface indicates statistical significance.
IQR, Interquartile range (25th quartile, 75th quartile).
*Steps 1 to 4, respectively, refer to second-generation H_1-antihistamines (2gAH), updosed up to 4-fold the standard dose of 2gAH, 2gAH with add-on omalizumab, and 2gAH with add-on cyclosporin.

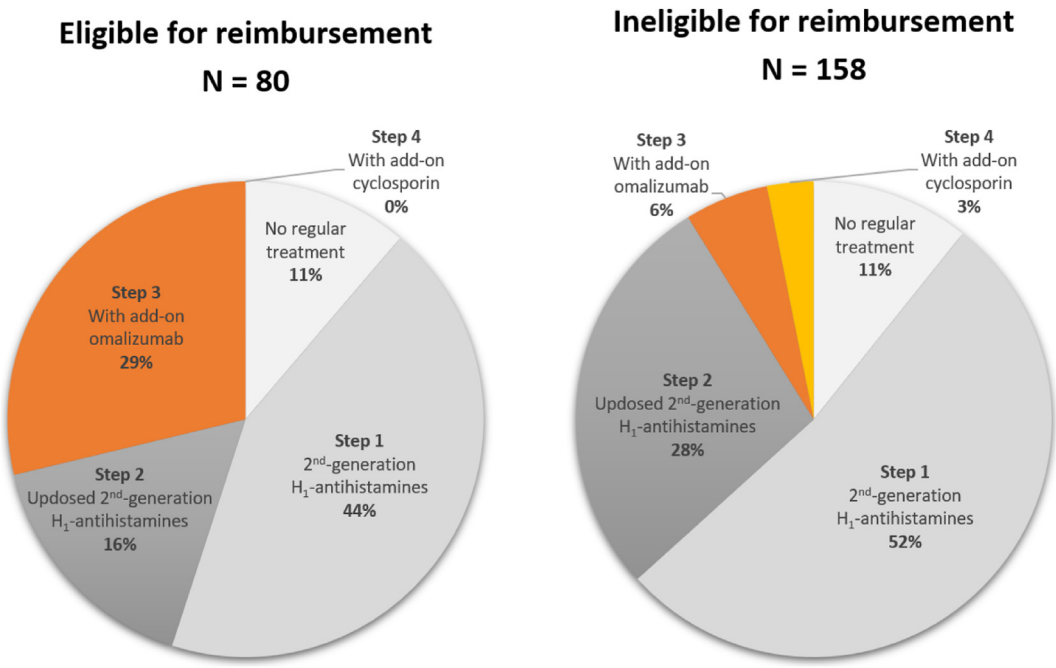

FIG 1. Distribution of CSU treatment steps according to drug eligibility status.

TABLE II. Multivariate analysis for factors affecting prescription of omalizumab

Factor	Odds ratio	95% CI	*P* value
Male sex	0.439	0.132-1.458	.179
Age of onset	0.982	0.958-1.006	.138
Self-reported triggers	2.298	0.922-5.726	.074
UAS7	**1.068**	**1.021-1.116**	**.004**
Drug eligibility status	**9.351**	**3.689-23.703**	**<.001**

Boldface indicates statistical significance.

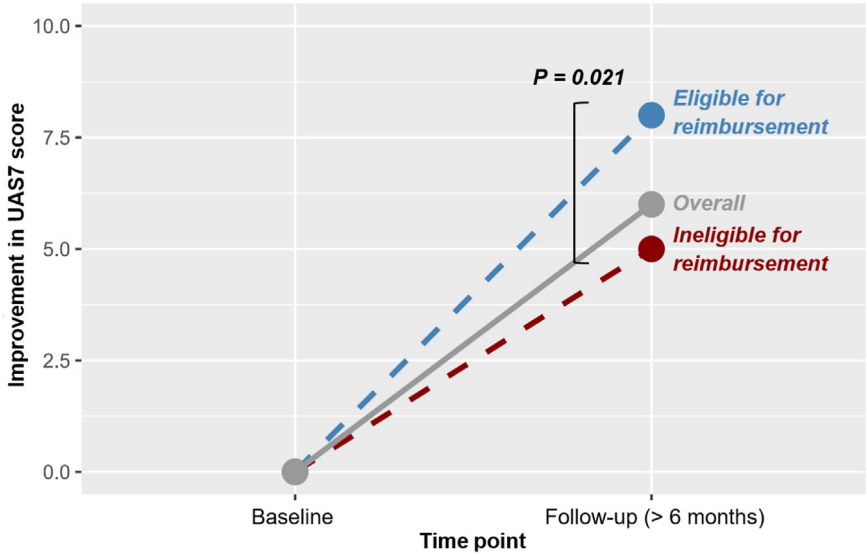

FIG 2. Improvement in UAS7 according to drug eligibility status.

This study highlights the importance of patient access and its independent association with use of biologics and disease control. The lower rate of omalizumab use (as well as dosing) with corresponding poorer disease control among patients ineligible for drug reimbursement, clearly demonstrates the disparity of CSU care between patients with differing medication accessibility. Recently, effects of other social determinants (such as race or geographic location of patients) have also been reported to

influence biologic use for patients with CSU, and it would be of interest to further delineate whether these were independent effects or rather, as in this present study, related to treatment accessibility (eg, reimbursable costs).[9] This study was limited by its observational nature and by the fact that we could not investigate other determinants such as education, employment, or income or patient outcomes beyond UAS7. Furthermore, all of our patients were Han Chinese (making up >90% of Hong Kong's population), which may limit the generalizability of our findings to ethnic minorities residing in the territory of Hong Kong.[10]

We strongly believe that disparities in treatment access also pertain to other populations and that such inequalities need to be addressed at a global level. All patients with CSU deserve equity in accessing the standard of care, which should not be limited by arbitrary or nonclinical eligibility criteria for drug reimbursement. We advocate for international, collaborative interventions and studies examining the importance of social determinants on CSU outcomes.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

Clinical implications: Ineligibility for drug reimbursement is associated with lower use of biologics in CSU, which translates into poorer disease control, thus warranting interventions to promote guideline-based CSU treatment and equity.

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