

Chronic spontaneous urticaria: a 16-year analysis of pediatric patient demographics, treatment patterns, and comorbidities

Sarah P Pourali¹ BS, Alison H Kohn² BS, Madison E Jones³ BA, April W Armstrong³ MD MPH

Affiliations: ¹Vanderbilt University School of Medicine, Nashville, Tennessee, USA, ²Charles E Schmidt College of Medicine, Florida Atlantic University, Boca Raton, Florida, USA, ³Keck School of Medicine, University of Southern California, Los Angeles, California, USA

Corresponding Author: April W Armstrong MD MPH, University of Southern California, 1975 Zonal Avenue, KAM 510, MC 9034, Los Angeles, CA 90089, Tel: 323-865-3871, Fax: 323-865-0699, Email: armstrongpublication@gmail.com

Keywords: chronic urticaria, idiopathic, National Ambulatory Medical Care Survey, population study, urticaria

To the Editor:

Chronic spontaneous urticaria is a mast-cell mediated disease, characterized by the formation of wheals with or without angioedema occurring multiple times a week for at least 6 weeks [1]. Chronic urticaria is estimated to have a prevalence of 0.1-0.3% in children [2]. The pathogenesis is multifactorial and potential triggers include autoimmunity, food sensitivities, and infections [2]. There is a paucity of information on outpatient encounters for urticaria in the pediatric population. We aim to examine patient demographics, treatment patterns, and comorbidities among children with chronic urticaria with an identifiable cause and idiopathic urticaria in the U.S.

We conducted a cross-sectional study from 2001-2016 using the National Ambulatory Medical Care Survey (NAMCS). The National Ambulatory Medical Care Survey is administered annually and reports nationally representative data on outpatient visits in the U.S. Visits are weighted to produce nationally representative samples. Visit weights are derived from a robust, multistep calculation including adjustment for probability of visit selection, adjustment for nonresponse, ratio adjustment, and weight smoothing. Chronic urticaria is defined as urticaria lasting more than 6 weeks; it is further classified as chronic urticaria with, versus without an

identifiable cause. We utilized ICD-9/ICD-10 coding to identify visits. Specifically, codes for “other urticaria—chronic urticaria” (708.8 and L50.8) identified visits with an identified cause and “idiopathic urticaria” (708.1 and L50.1) identified visits without an identified cause.

During this 16-year period, 403,812 chronic urticaria visits were conducted (**Table 1**). The majority of visits (92.8%) were for female patients. The average age of patients was 9.68±5.29 years. The most commonly reported comorbidities included asthma (30.8%), upper respiratory infections (11.2%), and angioedema (8.3%). Treatments for chronic urticaria included antihistamines (79.6%), leukotriene inhibitors (22.2%), and systemic corticosteroids (11.9%), (**Table 2**). The majority of visits were conducted by pediatricians (50.7%).

From 2001-2016, 447,895 visits occurred for idiopathic urticaria (**Table 1**). The majority of visits (54.8%) occurred for female patients. The average patient age was 9.78±5.71 years. The most common comorbidities included pruritus (14.2%), contact dermatitis (6.7%), and upper respiratory infections (3.5%). Treatments for idiopathic urticaria included antihistamines (68.3%) and systemic corticosteroids (13.6%). Most visits were conducted by pediatricians (50.4%).

Although the NAMCS survey design does not allow for the assessment of prevalence, the majority of visits occurred for female patients, which is consistent with previous epidemiological data on urticaria [2].

Table 1. Sociodemographics of National Ambulatory Medical Care Survey visits with diagnosis of chronic urticaria (708.8 & L50.8) and idiopathic urticaria (708.1 & L50.1).

	Chronic Urticaria		Idiopathic Urticaria	
	Total weighted visits	% of Total visits	Total weighted visits	% of total visits
Totals	403,812	100	447,895	100
Age, mean (±SD)	9.68 (±5.29)	-	9.78 (±5.71)	-
Sex				
Male	28,969	7.2	202,474	45.2
Female	374,843	92.8	245,421	54.8
Race & ethnicity				
Non-Hispanic White	222,279	55	299,343	66.8
Non-Hispanic Black	-	-	64,474	14.4
Hispanic	181,533	45	45,115	10.1
Non-Hispanic other	-	-	38,963	8.7
Providers				
Dermatologists	11,318	2.8	-	-
Pediatrics	204,815	50.7	225,856	50.4
Other	187,679	46.5	222,039	49.6
Comorbidities				
Asthma	124,383	30.8	7,218	1.6
URI	45,271	11.2	15,630	3.5
Angioedema	33,450	8.3	-	-
Rhinitis	19,661	4.9	7,790	1.7
Atopic conjunctivitis	1,335	0.3	6,666	1.5
Pruritus	414	0.1	63,449	14.2
Contact dermatitis	-	-	29,882	6.7

Comorbidities for chronic spontaneous urticaria include asthma, rhinitis, autoimmune diseases, and psychiatric disorders [2,3]. This study found asthma and rhinitis to be among the most common comorbidities. Finally, diagnoses related to urticaria, such as pruritus and angioedema, were also common comorbidities.

Antihistamines are first-line treatment for urticaria. However, half of patients do not improve with traditional dosing of antihistamines and many remain refractory despite up-dosing of

antihistamines [4]. Although not prescribed in this study, omalizumab is a biologic targeting immunoglobulin E that was approved in 2014 for patients over the age of 12 with chronic spontaneous urticaria unresponsive to antihistamine treatment [5]. It is associated with significant improvement in the signs and symptoms of urticaria and it also used to treat moderate-to-severe asthma.

Limitations of this study include the use of ICD coding, which does not allow clinicians to input more granular categories or divisions of different

Table 2. Medication prescribed for National Ambulatory Medical Care Survey visits with diagnosis of chronic urticaria (708.8 & L50.8) and idiopathic urticaria (708.1 & L50.1).

Medication Class	Chronic Urticaria		Idiopathic Urticaria	
	No. Visits with Medication Prescribed	% of Total Visits	No. Visits with Medication Prescribed	% of Total Visits
Antihistamines	321,439	79.6	305,755	68.3
Systemic steroids	47,975	11.9	61,027	13.6
Leukotriene Inhibitors	89,938	22.2	-	-

subtypes of urticaria. As with any database study using ICD codes, the possibility of misclassification exists.

In conclusion, this study revealed that most chronic and idiopathic urticaria visits occurring in the pediatric population were in female patients. A small percentage of visits were conducted by dermatologists, as compared to the larger proportion of visits conducted by pediatricians. Although patients may present first to pediatricians, difficult-to-manage forms of urticaria and comorbidities such as contact dermatitis may necessitate referral to dermatologists. Finally, omalizumab is the first biologic option for patients

with moderate to severe forms of chronic urticaria not managed by antihistamines [6,7]. We anticipate that with more innovations in drug development, patients with chronic urticaria will have greater choices and potentially better clinical outcomes.

Potential conflicts of interest

Dr. Armstrong has served as a research investigator and/or scientific advisor to AbbVie, BMS, Incyte, Leo, UCB, Janssen, Lilly, Novartis, Ortho Dermatologics, Sun, Dermavant, Dermira, Sanofi, Regeneron, Pfizer, and Modmed. SPP, AHK, and MEJ have no conflicts of interest to declare.

References

1. Kaplan AP, Giménez-Arnau AM, Saini SS. Mechanisms of action that contribute to efficacy of omalizumab in chronic spontaneous urticaria. *Allergy*. 2017;72:519-533. [PMID: 27861988].
2. Church MK, Weller K, Stock P, Maurer M. Chronic spontaneous urticaria in children: itching for insight. *Pediatr Allergy Immunol*. 2011;22:1-8. [PMID: 21261741].
3. Isik SR, Karakaya G, Celikel S, Demir AU, Kalyoncu AF. Association between asthma, rhinitis and NSAID hypersensitivity in chronic urticaria patients and prevalence rates. *Int Arch Allergy Immunol*. 2009;150:299-306. [PMID: 19494528].
4. Maurer M, Weller K, Bindslev-Jensen C, et al. Unmet clinical needs in chronic spontaneous urticaria. A GA²LEN task force report. *Allergy*. 2011;66:317-330. [PMID: 21083565].
5. Genentech I. Xolair (Omalizumab) Package Insert. In:2020.
6. Kanters TA, Thio HB, Hakkaart L. Cost-effectiveness of omalizumab for the treatment of chronic spontaneous urticaria. *Br J Dermatol*. 2018;179:702-708. [PMID: 29476533].
7. Rubini NPM, Ensina LFC, Silva EMK, Sano F, Solé D. Effectiveness and safety of Omalizumab in the treatment of chronic spontaneous urticaria: Systematic review and meta-analysis. *Allergol Immunopathol (Madr)*. 2019;47:515-522. [PMID: 31607407].