



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Urticaria after COVID-19 vaccination and vaccine hesitancy

Allen Judd, BA^a, Upeka Samarakoon, PhD, MPH^a,
Anna R. Wolfson, MD^{a,b}, Aleena Banerji, MD^{a,b},
Esther E. Freeman, MD, PhD^{b,c,*}, and
Kimberly G. Blumenthal, MD, MSc^{a,b,*}



Clinical Implications

Of 271 survey respondents from the Massachusetts General Hospital Vaccine Allergy Registry who experienced urticaria after coronavirus disease 2019 (COVID-19) vaccination, most reported that they would be unlikely to receive future recommended COVID-19 vaccine doses, despite largely believing COVID-19 vaccines are safe.

The ongoing coronavirus disease 2019 (COVID-19) pandemic affects millions of people annually, but vaccination efforts remain limited by vaccine hesitancy.¹ Prior study of primary COVID-19 vaccination demonstrated that individuals who experience postvaccination allergic signs or symptoms, including urticaria, are less likely to complete all recommended COVID-19 vaccine doses.^{2,3} However, most vaccine reactions are not a contraindication to subsequent vaccination.

Although cutaneous reactions after COVID-19 vaccination vary in onset timing, clinical presentation, and severity, urticaria has been a common presentation after COVID-19 vaccination,^{4,5} and some urticaria has lasted more than 6 weeks (ie, chronic urticaria).⁶ We sought to quantify the impact of urticaria after COVID-19 vaccination on quality of life and vaccine hesitancy.

The Massachusetts General Hospital COVID-19 Vaccine Allergy Registry solicits self-reports of postvaccination allergic and cutaneous reactions following COVID-19 vaccines via an online case form.⁷⁻¹⁰ The survey is available to the public and was advertised through allergist networks, lay press, and social media. The case form includes questions about COVID-19 vaccine hesitancy; in cases of reported urticaria, the form includes questions from the Urticaria Control Test (UCT), a validated 4-question scale for quality of life and urticaria management.^{10,11} Cases of urticaria (“hives at the injection site,” “hives at location other than the injection site,” and/or “skin writing [redness and/or hives where you scratch your skin, known as dermatographism]”) were summarized from March 13 to September 1, 2022. Unanswered questions were considered “unknown.” Mean UCT scores were calculated, and all scores were grouped on the basis of established criteria: a recommended cutoff value of 11 or less achieves greatest sorting accuracy; a cutoff value of 8 or less achieves specificity of more than 90% (ie, negative for well-controlled urticaria).¹¹

We identified 271 cases of urticaria after COVID-19 vaccination (Table I). Most respondents became aware of the registry through social media (n = 139 [51%]), and other avenues of

TABLE I. Demographic characteristics of self-reported urticaria cases

Characteristic (n = 271)	Subcategory	Respondents, n (%)
Age (y)	Mean ± SD	36 ± 13
Age categories (y)	≤20	8 (3)
	21-30	110 (41)
	31-40	70 (26)
	41-50	44 (16)
	51-60	18 (7)
	61-70	17 (6)
	71-80	3 (1)
	81-90	1 (<1)
Sex	Female	200 (74)
	Male	71 (26)
Race	Asian	23 (8)
	Black	5 (2)
	Multiple	13 (5)
	Prefer not to answer/unknown	8 (3)
	White	222 (82)
Ethnicity	Not Hispanic/Latino	230 (85)
	Hispanic/Latino	30 (11)
	Prefer not to answer/unknown	11 (4)
Reaction dose	Dose 1	12 (4)
	Dose 2	21 (8)
	Dose 3	221 (82)
	Dose 4	10 (4)
	Unknown	7 (3)
Reaction onset timing	<24 h	15 (6)
	24 h-1 wk	22 (8)
	1 wk-2 wk	181 (67)
	>2 wk	47 (17)
	Do not know/unknown	6 (2)
	Took medication for urticaria	229 (85)
	Urticaria ongoing at report*	247 (91)

*Of those who reported resolved symptoms (n = 15), 53% (n = 8) reported reaction duration >1 mo.

referral included our study website (n = 26 [10%]) and news articles (n = 15 [6%]). Cases (mean, 36 ± 13 years, 74% female, 82% White, 11% Hispanic) largely reported urticaria after the third (booster) dose of vaccine (n = 221 [82%]), with onset more than 24 hours after vaccination (n = 250 [92%]), requiring medication (n = 229 [85%]). A total of 247 (91%) had ongoing urticaria at the time of their survey completion.

Of 265 respondents who completed the UCT, mean score was 6 ± 4 (Table II). A total of 234 (88%) respondents scored 11 or

TABLE II. Quality of life, urticaria control, and vaccine hesitancy

		Respondents, n (%)	
UCT (n = 265)*		Mean score 6 ± 4	
		Score ≤11†	234 (88)
		Score ≤8‡	204 (77)
How much have you suffered from the physical symptoms of the urticaria (itch, hives [welts], and/or swelling) in the last 4 weeks?	[0] Very much	120 (44)	Very much or much, n (%)
	[1] Much	77 (28)	
	[2] Somewhat	42 (15)	
	[3] A little	18 (7)	
	[4] Not at all	12 (4)	
		197	(73)
How much was your quality of life affected by the urticaria in the last 4 weeks?	[0] Very much	92 (34)	Very much or much, n (%)
	[1] Much	73 (27)	
	[2] Somewhat	60 (22)	
	[3] A little	31 (11)	
	[4] Not at all	13 (5)	
		165	(61)
How often was the treatment for your urticaria in the last 4 weeks not enough to control your urticaria symptoms?	[0] Very much	51 (19)	Very much or much, n (%)
	[1] Much	61 (23)	
	[2] Somewhat	77 (28)	
	[3] A little	36 (13)	
	[4] Not at all	43 (16)	
		112	(41)
Overall, how well have you had your urticaria under control in the last 4 weeks?	[0] Not at all	41 (15)	Not at all or a little, n (%)
	[1] A little	61 (23)	
	[2] Somewhat	83 (31)	
	[3] Well	54 (20)	
	[4] Very well	30 (11)	
		102	(38)
Vaccine hesitancy questions (n = 271)		Respondents, n (%)	
If additional COVID-19 vaccinations are recommended in the future, how likely or unlikely would you be to get the [next] coronavirus vaccination?‡	Very likely	27 (10)	Very unlikely or unlikely, n (%)
	Likely	43 (16)	
	Unlikely	78 (29)	
	Very unlikely	108 (40)	
	Unknown	15 (6)	
		186	(69)
Please select the answer that best fits your agreement with the following statement: information on side effects following immunization is discussed openly by the government and public health officials.	Very much	21 (8)	A little or not at all, n (%)
	Much	23 (8)	
	Somewhat	54 (20)	
	A little	79 (29)	
	Not at all	70 (26)	
		149	(55)
In general, how safe do you think the COVID-19 vaccines are?	Very safe	45 (17)	Somewhat unsafe or very unsafe, n (%)
	Safe	115 (42)	
	Somewhat unsafe	61 (23)	
	Very unsafe	8 (3)	
	Not sure	24 (9)	
		69	(25)
		18	(7)

*A total of 6 participants did not answer all UCT questions and were excluded from scoring. Unknown responses: first question (n = 2 [1%]); second question (n = 2 [1%]); third question (n = 3 [1%]); fourth question (n = 2 [1%]).

†Weller et al¹¹ recommends a value of ≤11 for poorly controlled urticaria, demonstrating the greatest rate of correct category classification. A value of ≤8 represents specificity >90% (ie, negative for well-controlled urticaria).

‡Respondents who answered *Very unlikely* or *Unlikely* (n = 186) were presented a follow-up question, “Please select the explanation(s) that best describes your reasoning for being unlikely or very unlikely to get another COVID vaccine [Check all that apply],” and the 3 most selected choices were as follows: *My skin-related side effects from vaccination*, n = 178 (96%); *I am worried about unknown future effects of the vaccine*, n = 51 (27%); and *I feel adequately protected (prior natural infection and/or prior shots)*, n = 45 (24%).

less on the UCT, and 204 (77%) scored 8 or less. Most indicated “Much” or “Very much” that they have suffered from urticaria (n = 197 [73%]) and that urticaria affected their quality of life (n = 165 [61%]). Most respondents reported that they would not receive future COVID-19 vaccine doses even if recommended (n = 186 [69%]), nearly all (178 of 186 [96%]) implicating their skin-related side effects. Most respondents (n = 149 [55%]) indicated that information on side effects

following immunization was insufficiently openly discussed by government and public health officials. However, only 69 (25%) respondents believed that the COVID-19 vaccines were generally unsafe.

Across 271 self-reported cases of urticaria after COVID-19 vaccination in a national institutionally supported case registry, most respondents had poorly controlled urticaria substantially impacting their quality of life. Urticaria has been previously shown

as a common cutaneous reaction after COVID-19 vaccination.^{4,5} Although the incidence of chronic urticaria after COVID-19 vaccination is not currently known, cases have been reported in medical literature,⁶ and thousands of patients belong to online support groups for this condition.¹² We found that urticaria after COVID-19 vaccination was comparably morbid and impactful on quality of life compared with previous studies of chronic urticaria.¹³

We identified that individuals with postvaccination urticaria may be unwilling to receive future recommended COVID-19 vaccine doses. These results expand on previous data in health care employees who reported postvaccination allergic signs or symptoms, demonstrating an increased risk of incomplete vaccination between 500% and 1000%.^{2,3} In our study, individuals with urticaria after COVID-19 vaccination reported that, despite their vaccine hesitancy, they believed that the vaccines were safe. As such, feelings of vaccine hesitancy appear to be spurred by a sense of personal protection from a poorly understood reaction, rather than a newly onset distrust of the COVID-19 vaccines resulting from their reaction. Our findings support the need for further in-depth immunologic research into postvaccination urticaria and the importance of the Allergy and Immunology community's dissemination of evidence-based information to address patient concerns.¹⁴

Our data were self-reported and unverified and therefore subject to misclassification. Given the cross-sectional nature of this registry, chronic urticaria could not be fully assessed. However, most cases reported ongoing urticaria, and approximately 1 in 5 cases had progressed to chronic urticaria at the time of reporting. Although vaccine manufacturer was not available in this data set, the patient-reported registry overall includes 95% mRNA vaccines from Pfizer-BioNTech or Moderna.¹⁰ In addition, because the case registry was hosted on an institutional website and publicized through allergist networks, lay press, and social media, a response rate cannot be determined, and a potential respondent bias may exist if more severe cases of urticaria are more likely to be reported. Participants were most likely to report reactions to their third dose of vaccination (a booster dose) due to the time frame of data collection for this study, introducing ascertainment bias.

Studying the etiology, outcomes, recurrence, management, and patient education regarding urticaria after COVID-19 vaccination will be critical to reducing vaccine hesitancy.

^cDepartment of Dermatology, Massachusetts General Hospital, Boston, Mass

^{*}Denotes shared senior authorship.

No funding was received to support the conduct of this work.

Conflicts of interest: The authors have no conflicts of interest to disclose.

Received for publication October 14, 2022; revised November 23, 2022; accepted for publication December 8, 2022.

Available online December 26, 2022.

Corresponding author: Kimberly G. Blumenthal, MD, MSc, Massachusetts General Hospital, The Mongan Institute, 100 Cambridge St, 16th Fl, Boston, MA 02108.

E-mail: e-kblumenthal@mgh.harvard.edu.

2213-2198

© 2022 American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaip.2022.12.010>

REFERENCES

- Shakeel CS, Majeed AA, Mirza MS, Chaudhry B, Khan SJ. Global COVID-19 vaccine acceptance: a systematic review of associated social and behavioral factors. *Vaccines (Basel)* 2022;10:110.
- Robinson LB, Landman AB, Shenoy ES, Hashimoto D, Fu X, Camargo CA Jr, et al. Allergic symptoms after mRNA COVID-19 vaccination and risk of incomplete vaccination. *J Allergy Clin Immunol Pract* 2021;9:3200-3202.e1.
- Al-Obaydi S, Hennrikus E, Mohammad N, Lehman EB, Thakur A, Al-Shaikhly T. Hesitancy and reactogenicity to mRNA-based COVID-19 vaccines—early experience with vaccine rollout in a multi-site healthcare system. *PLoS One* 2022;17:e0272691.
- Prasad S, McMahon DE, Tyagi A, Ali R, Singh R, Rosenbach M, et al. Cutaneous reactions following booster dose administration of COVID-19 mRNA vaccine: a first look from the American Academy of Dermatology/International League of Dermatologic Societies registry. *JAAD Int* 2022;8:49-51.
- Tan SW, Tam YC, Pang SM. Cutaneous reactions to COVID-19 vaccines: a review. *JAAD Int* 2022;7:178-86.
- Wolfson AR, Freeman EE, Blumenthal KG. Urticaria 12 days after COVID-19 mRNA booster vaccination. *JAMA* 2022;327:1702-3.
- Mass General Allergy Research. COVID-19 Vaccine Allergy Registry. Accessed January 9, 2022. <https://allergyresearch.massgeneral.org/>.
- Anvari S, Samarakoon U, Fu X, Jaggers J, Gonzalez-Estrada A, Chong HJ, et al. Urticaria and/or angioedema secondary to mRNA COVID-19 vaccines: updates from a United States case registry. *Allergy* 2023;78:283-6.
- Jaggers J, Samarakoon U, Fu X, Gonzalez-Estrada A, Anvari S, Chong HJ, et al. Anaphylaxis after COVID-19 vaccination: a registry-based study. *J Allergy Clin Immunol Pract* 2022;10:3020-3.
- Judd A, Samarakoon U, Blumenthal KG. Self-reported reactions after COVID-19 vaccination (abstract). *J Allergy Clin Immunol Pract* 2022;149. Supp AB56.
- Weller K, Groffik A, Church MK, Hawro T, Krause K, Metz M, et al. Development and validation of the Urticaria Control Test: a patient-reported outcome instrument for assessing urticaria control. *J Allergy Clin Immunol* 2014;133:1365-1372.e1-6.
- Chronic Spontaneous Urticaria After COVID-19 Vaccine Support Group. Accessed January 9, 2023. <https://www.facebook.com/groups/442950024085956/about/>.
- Wagner N, Zink A, Hell K, Reinhardt M, Romer K, Hillmann E, et al. Patients with chronic urticaria remain largely undertreated: results from the DERMLINE online survey. *Dermatol Ther (Heidelb)* 2021;11:1027-39.
- Turner PJ, Larson H, Dubé É, Fisher A. Vaccine hesitancy: drivers and how the allergy community can help. *J Allergy Clin Immunol Pract* 2021;9:3568-74.

^aDivision of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, Mass

^bHarvard Medical School, Boston, Mass