# New-onset chronic spontaneous urticaria post–COVID-19 vaccination—South African case series

**Valmy Craffert, MBChB, BSc, Dip HIV Man,[a] Cascia Day, MBBCh, FCP, MMed, Dip HIV Man,[a,b] and Jonny Peter, MBChB, FCP, MMed, PhD[a,b]** *Cape Town, South Africa*

**Background: Chronic spontaneous urticaria (CSU) is defined as the spontaneous occurrence of hives, angioedema, or both for more than 6 weeks; several inciting triggers including vaccines have been implicated. Coronavirus disease 2019 (COVID-19) vaccinations have been well tolerated by patients with CSU. However, reports have emerged of CSU triggered by COVID-19 vaccination and this study describes a South African case series.**
**Objective: To provide details of the first case series of new-onset CSU post–COVID-19 vaccination in Africa and summarize the global literature of reported cases to date.**
**Methods: All patients referred to our Urticaria Center of Excellence in Cape Town from the initiation of the COVID-19 vaccine rollout in South Africa (from February 2021 to August 2022) were reviewed to identify patients who developed new-onset CSU within 12 weeks of receiving a COVID-19 vaccine. Medical history, physical examinations, and laboratory investigations were reviewed.**
**Results: More than 20 million adults received COVID-19 vaccinations in South Africa during the study period. Eight patients had new-onset chronic urticaria post–COVID-19 vaccination; 6 of the 8 patients were female, the median age was 41 years (interquartile range [IQR], 38-44), and all had a history of atopy. Only 1 reported COVID-19 infection post vaccination. Chronic urticaria occurred following Pfizer-BioNTech, AstraZeneca, and Janssen Ad26.COV2.S vaccination in 6, 1, and 1 patient, respectively, with a median of 12 days (IQR, 3-38) from vaccination to symptoms onset. The baseline median score for Urticarial Activity Score 7 was 34 (IQR, 29-40), and 5 of the 8 patients (63%) had a total IgE level of more than 43 IU/L. All patients received high-dose antihistamines, with only 3 patients controlled.**
**Conclusions: New-onset CSU can rarely be triggered by COVID-19 vaccinations, most commonly mRNA vaccines. COVID-19 vaccine–triggered CSU appears to have a phenotype similar to that triggered by other inciting agents and across populations. (J Allergy Clin Immunol Global 2023;2:100154.)**

***Key words:*** *Chronic spontaneous urticaria, COVID-19 vaccine, COVID-19 vaccine allergy, new-onset CSU*

Chronic spontaneous urticaria (CSU) is a mast cell–driven disease characterized by the spontaneous occurrence of hives (wheals), angioedema, or both for a duration of more than 6 weeks.[1] Its pathophysiology is not fully understood; however, current accepted mechanisms include IgE and IgG autoantibodies, which predispose to mast cell and basophil activation, and involvement of coagulation and complement cascades.[2] Ongoing chronic urticaria can have a profound negative impact on a patient's quality of life.[3] Several risk factors have been described for chronic urticaria, but strong causal relationships are limited. In contrast to acute urticaria, in which infections and drugs are the commonest associated triggers, chronic urticaria is most commonly associated with autoimmune diseases (AIDs), particularly autoimmune thyroiditis.[4,5] Atopic diseases have also been identified as risk factors, as well as several states associated with chronic low-grade inflammation, for example, obesity, vitamin D deficiency, chronic infections such as *Helicobacter pylori*, and malignancy.[2,6] Vaccinations, although not a clearly established risk factor for CSU, have been associated with the development of CSU. These include vaccines against hepatitis B virus, human papillomavirus, influenza, yellow fever, and diphtheria-tetanus-pertussis.[7]

The coronavirus disease 2019 (COVID-19) pandemic has led to an estimated 649 million infections, and the world's largest vaccine rollout, with 13 billion vaccine doses given to date.[8,9] Cutaneous manifestations during severe acute respiratory syndrome coronavirus 2 infection have been well described, with prevalence between 0.2% and 20.4%.[10] Reported dermatological clinical patterns include the following: pseudo-chilblain; vesicular, urticarial, and maculopapular rashes; livedo/necrosis; vasculitides; pityriasis rosea– and erythema multiforme–like rashes; and others.[10-12] Acute urticarial eruptions, along with angioedema in certain cases, have occurred before, during, or after the onset of systemic symptoms, and all have resolved within 6 weeks.[13] At the time of writing, there was no available literature describing new-onset CSU post–COVID-19 infection, only the exacerbation of symptoms in a fifth of known patients with CSU.[14,15] However, in the authors' experience, new-onset CSU can occur post–COVID-19 infection. Various studies have described cutaneous reactions post–COVID-19 vaccination and, after local injection-site reactions, urticaria and angioedema are the most common cutaneous adverse events.[16-18] Most of these reactions start more than 24 hours post vaccination and are self-limiting before 6 weeks.

From [a]the Allergy and Immunology Unit, University of Cape Town Lung Institute, Mowbray, Cape Town; and [b]the Division of Allergology and Clinical Immunology, Department of Medicine, Faculty of Health Sciences, Groote Schuur Hospital, Observatory, Cape Town.

Received for publication December 15, 2022; revised May 19, 2023; accepted for publication May 24, 2023.

Available online July 24, 2023.

Corresponding author: Jonny Peter, MBChB, FCP, MMed, PhD, Allergy and Immunology Unit, University of Cape Town Lung Institute, George Street, Mowbray, 7700, Cape Town, PO Box 34560, Groote Schuur, 7937, South Africa. E-mail: jonny.peter@uct.ac.za.

The CrossMark symbol notifies online readers when updates have been made to the article such as errata or minor corrections

2772-8293



https://doi.org/10.1016/j.jacig.2023.100154

*Abbreviations used*
AID: Autoimmune disease
CIndU: Chronic inducible urticaria
COVID-19: Coronavirus disease 2019
CSU: Chronic spontaneous urticaria
ESR: Erythrocyte sedimentation rate
IQR: Interquartile range

In this article, we detail the first case series of chronic urticaria post–COVID-19 vaccination in Africa and summarize the global literature of reported cases to date. Although rare, allergists and dermatologists need to be alerted to this phenomenon, especially given the development and continued rollout of new COVID-19 vaccinations.

## METHODS

UCARE/ACARE (Urticaria Centers of Reference and Excellence/Angioedema Centers of Reference and Excellence) is currently the only center of excellence for patients with urticaria in Africa, with referral from both Cape Town and other parts of South Africa. During the COVID-19 vaccine rollout, one of the authors (J.P.) had served on the National Immunisation Safety Executive Committee, which reviews all vaccine-related adverse events reported to the South African Health Pharmacy Regulatory Authority. Using these mechanisms, patients who developed new-onset chronic urticaria within 12 weeks of receiving a COVID-19 vaccine during the South African rollout (from February 2021 to August 2022) were identified. Demographic information, medical history, response to therapy, physical examination, and available laboratory investigations were reviewed by clinic physicians. This study was approved by the University of Cape Town Human Research Ethics Committee (HREC633/2018).

CSU was diagnosed and assessed according to the European Academy of Allergology and Immunology guidelines. Demographic information collected included age, sex, and Fitzpatrick skin tone. Important medical history included comorbidities, allergic history, history of previous COVID-19 infection, COVID-19 vaccination history, and specific history related to urticaria and/or angioedema post–COVID-19 vaccination. When available, scores for the Urticarial Activity Score 7 and the Chronic Urticaria Quality of Life questionnaires were collected. Physical examination findings collected were height, weight, and any evidence of allergic disease or AID. Laboratory investigations related to risk factors for CSU and autoallergy versus autoimmune CSU phenotypes included $HbA_{1c}$, thyroid and other autoantibodies, total IgE and eosinophilia, and evidence of chronic infections such as elevated erythrocyte sedimentation rate (ESR) and specific infections including HIV and *H pylori*.

## RESULTS

During the South African COVID-19 vaccine rollout, 37 million vaccines had been administered, with 51.7% of the adult population vaccinated.[19] Tables I and II provide details of and the summary statistics for the 8 patients who developed new-onset chronic urticaria within 12 weeks post–COVID-19 vaccination. Most were female (n = 6 [75%]), with a median age of 41 years (interquartile range [IQR], 38-44), and cases involved all Fitzpatrick skin tones. Two patients developed cholinergic chronic inducible urticaria (CIndU), whereas the other patients had CSU. One of the patients with CSU had associated cholinergic CIndU. Of the 6

**TABLE I.** Description of patients who developed new-onset CSU/CIndU post–COVID-19 vaccination

| Age (y) | Sex | Fitzpatrick skin tone type | Medical history/ comorbidities | Allergy history | CSU post | Time of onset post–COVID-19 vaccination (d) | Vaccine | CSU vs CIndU |
|---|---|---|---|---|---|---|---|---|
| 40 | Male | II | Obesity | Atopic dermatitis | Second dose | 30 | Pfizer-BioNTech | CIndU (cholinergic) |
| 32 | Female | III | Peptic ulcer disease | Allergic rhinitis, contact dermatitis (nickel, chrome), childhood atopic dermatitis | First dose | 1 | Pfizer-BioNTech | CSU |
| 39 | Male | III | Childhood leukemia | Allergic rhinitis, penicillin allergy | Second dose | 60 | Pfizer-BioNTech | CSU |
| 41 | Female | IV | Staphylococcus colonization | Atopic dermatitis | First dose | 14 | Pfizer-BioNTech | CSU and CIndU (cholinergic) |
| 38 | Female | IV | GORD, previous GSW both legs | Allergic rhinitis, atopic dermatitis, asthma | Second dose | 44 | Pfizer-BioNTech | CSU |
| 45 | Female | V | Nil | Allergic rhinitis | First dose | 2 | Janssen | CSU |
| 64 | Female | II | Osteoporosis, rheumatoid arthritis, NAFLD, depression | Aquagenic pruritis | First dose | 10 | Pfizer-BioNTech | CSU |
| 42 | Female | III | Osteopenia | Childhood atopic dermatitis, peanut allergy | First dose | 7 | Astra Zeneca Janssen | CIndU (cholinergic) |

*GORD*, Gastroesophageal reflux; *GSW*, gun shot wound; *NAFLD*, nonalcoholic fatty liver disease.

**TABLE II.** Summary statistics of patients who developed new-onset CSU or CIndU post–COVID-19 vaccination

| Variable | Value |
|---|---|
| Age (y), median (IQR) | 41 (38-44) |
| Sex, female, n (%) | 6 (75) |
| Allergy history, n (%) | |
| Allergic rhinitis | 5 (63) |
| Atopic dermatitis | 5 (63) |
| Contact dermatitis | 1 (13) |
| Drug allergy (penicillin) | 1 (13) |
| Food allergy | 1 (13) |
| COVID-19 infection before vaccination, n (%) | 0 (0) |
| COVID-19 infection postvaccination, n (%) | 1 (13) |
| Type of vaccine, n (%) | |
| Pfizer-BioNTech | 6 (75) |
| Janssen | 1 (13) |
| AstraZeneca | 1 (13) |
| Diagnosis, n (%) | |
| CSU | 6 (75) |
| CIndU | 2 (25) |
| UAS7 score, n = 6, median (IQR) | 34 (29-40) |
| CU-QoL score, n = 4, median (IQR) | 62 (43-72) |
| Symptoms, n (%) | |
| Urticaria only | 2 (25) |
| Angioedema only | 1 (13) |
| Urticaria and angioedema | 5 (63) |
| Time (d) from vaccination to symptoms, median (IQR) | 12 (3-38) |
| Time (d) from symptoms onset till diagnosis, median (IQR) | 105 (60-233) |
| Duration (mo) of symptoms to date (IQR) | 20 (10-23) |
| BMI, n = 6 | 30 (25-36) |
| Investigations | |
| Total IgE (IU/L), n = 8, median (IQR) | 172.5 (15.3-736.3) |
| Elevated IgE > 43 (IU/L), n = 8 (%) | 5 (63) |
| Eosinophil count ($\times 10^9$/L), n = 7, median (IQR) | 0.15 (0.04-0.24) |
| Eosinophilia | 0 |
| Deranged thyroid function, n = 8 | 0 |
| Elevated thyroid autoantibodies, n = 7 | 0 |
| Vitamin D deficiency, n = 5 (%) | 2 (40) |
| Elevated ESR (mm/h), n = 6 (%) | 1 (16.7) |
| Positive ANA, n = 7 | 0 |
| Abnormal serum protein electrophoresis, n = 7 | 1 (16.7) |
| Elevated tryptase (1-15 μg/L), n = 4 | 0 |
| Treatment | |
| High-dose antihistamines | 8 (100%) |
| Montelukast | 4 (50%) |
| No response to treatment | 0 |
| Partial response to treatment | 5 (63%) |
| Complete resolution on first-line treatment | 1 (12.5%) |
| Complete resolution, subsequently off-treatment | 2 (25%) |

*ANA*, Antinuclear antibody; *BMI*, body mass index; *CU-QoL*, Chronic Urticaria Quality of Life; *UAS7*, Urticarial Activity Score 7.

patients with CSU, 4 had both urticaria and angioedema, 1 had isolated urticaria, and 1 had isolated angioedema. All patients had a history of atopy, with 4 patients reporting multiple atopic diseases, most frequently allergic rhinitis (n = 5) and atopic dermatitis (n = 5). However, none of the patients had had anaphylaxis or previous adverse reactions to vaccines. One patient had a history of quiescent rheumatoid arthritis, but no other AIDs were noted. Only 1 patient acquired COVID-19 infection, which was mild. Infection occurred post vaccination and did not have an impact on CSU symptomatology. Five patients reported symptoms after receiving their first COVID-19 vaccine and 3 after their second dose of the vaccine. Three patients received subsequent vaccine doses, and all 3 experienced CSU flares. The mRNA Pfizer-BioNTech vaccine was most frequently implicated (n = 6 [75%]), but there were single cases of both adenovirus vector vaccines (AstraZeneca and Janssen Ad26.COV2.S). The median time from vaccination to onset of symptoms was 12 days (IQR, 3-38 days); however, the time from symptom onset to diagnosis was prolonged, with a median of 105 days (IQR, 60-233 days). Initial scores for Urticarial Activity Score 7 were available for 6 patients, with a median score of 34 (IQR, 29-40), indicating severe baseline disease activity. Body mass index values were available for 6 patients (median, 30 [IQR, 25-36]), with only 1 patient having a normal body mass index (16.7%), whereas 2 were overweight (33.3%) and 3 were obese (50%).

Laboratory results are presented in Table II. All patients had normal white cell counts and eosinophil counts (median, $0.15 \times 10^9$ [IQR, 0.04-0.24]), with 5 patients having an elevated total IgE level (>43 IU/L; median, 88.7 g/L [IQR, 10.25-504.5 g/L]). Only 1 patient had a mildly elevated ESR. All patients had negative autoantibodies, were euthyroid, and none had antithyroid peroxidase antibodies in the serum. All patients were HIV-negative, and only 1 patient had a positive IgG for *H pylori*. One patient had elevated free κ light chains on serum protein electrophoresis, and 2 were diagnosed with a vitamin D deficiency.

All patients were started on high-dose second-generation $H_1$ antihistamine (at 4 times the daily dose); only 2 patients achieved complete control on this therapy, 5 patients had a partial response to therapy, and 1 patient was unresponsive. The patient with no initial response was diagnosed with cholinergic urticaria and experienced symptom improvement when there was a change from cetirizine to fexofenadine. This did, however, coincide with a seasonal change from spring to winter. In addition, this patient's symptoms fully resolved after 7 months, and he has subsequently stopped all therapy. Four of the patients with only partial response were also initiated on montelukast therapy. One patient had a good response to dual therapy, whereas the other 3 achieved only mild additional symptom relief. Subsequently, 1 patient is awaiting approval for omalizumab therapy, 1 patient is part of a clinical trial for CSU with remibrutinib as the active therapy, and 2 other patients are awaiting enrollment in a clinical trial for barzolvolimab in CSU. Of note, the treatment of comorbid conditions identified (vitamin D deficiency and *H pylori* infection) did not improve the CSU symptoms.

## DISCUSSION

Chronic urticaria is a prevalent condition occurring across the world. Despite a growing understanding of the pathogenesis of both CSU and CIndU, the inciting events and pathways are poorly understood.[2] Uncommonly, vaccination has been implicated as an inciting event in new-onset CSU.[7] Thus, the mass COVID-19 vaccination effort, with more than 13 billion doses administered worldwide, represents a unique opportunity to consider vaccines as CSU triggers. Fortunately, COVID-19 vaccination seems to be a very rare trigger for new-onset CSU. Table III[20-29] provides a summary of the available literature, and our case series of 8 patients contributes to this knowledge base. In contrast, a multinational study of 2769 patients with preexisting chronic urticaria noted that vaccination exacerbated urticaria in approximately 16% of patients.[30]

The profile of our patients with CSU post vaccination is consistent with that in other case reports and series, with a

**TABLE III.** Summary of CSU case reports and series available in the literature

| Publication | Country | COVID-19 vaccine | Vaccine type | No. of cases | CSU post | Delay of onset | Treatment | Resolution | Sex | Age (y) | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| de Montjoye et al[20] | Belgium | Moderna | mRNA | 1 | First dose | 2 days | Anti-$H_1$, sCS, cyclosporine | No | Female (75%) | 56.5 (median) | Authors postulate that CSU onset in this case series not linked to AID |
| | | AstraZeneca | VV | 4 | First and second doses | 1-15 days | Anti-$H_1$, omalizumab | 75% | | | No history of previous COVID-19 infection |
| | | Pfizer-BioNTech | mRNA | 3 | First dose | 7-18 days | Anti-$H_1$, sCS, omalizumab | 67% | | | |
| Magen et al[21] | Israel | Pfizer-BioNTech | mRNA | 32 | Not noted | Not noted | Not discussed | Not discussed | Female (65.6%) | 41.2 (mean) | No statistically significant associations in the new-onset CSU group |
| Thomas et al[22] | United States | Pfizer-BioNTech | mRNA | 1 | Second dose | 7 days | Anti-$H_1$ | Symptom control but no resolution | Male | Early 20s | New-onset CSU after second dose of vaccine<br>No previous COVID-19 infection diagnosed |
| Adame et al[23] | United States | Pfizer-BioNTech | mRNA | 1 | First dose | 7 hours | Anti-$H_1$, sCS | Symptom control but no resolution | Female | 35 | Patient has concomitant Hashimoto disease, asthma, allergic rhinitis, and Ehlers-Danlos syndrome<br>No previous COVID-19 infection diagnosed |
| Brooks et al[24] | Canada | AstraZeneca | VV | 1 | First dose | 5 days | Anti-$H_1$, sCS, tCS | Yes | Male | 60 | Asthma, environmental allergies<br>COVID-19 infection not mentioned |
| Suan and Lee[25] | Australia | AstraZeneca | VV | 1 | Second dose | 14 days | Anti-$H_1$, sCS | Good symptom control but no resolution | Male | 39 | No concomitant illness<br>COVID-19 infection not mentioned |
| Pescosolido et al[26] | Switzerland | Pfizer-BioNTech | mRNA | 2 | Second or third dose | 30 days | Not mentioned | Not mentioned | Female (61%) | 44.4 (mean) | 22% history of atopy<br>Authors suggest allergic pathophysiology |
| | Switzerland | Moderna | mRNA | 30 | Third dose | 4-34 days | Anti-$H_1$, sCS | Improvement but no resolution | | | Only 4 cases of known previous COVID-19 infection |
| Strahan et al[27] | United States | Pfizer-BioNTech | mRNA | 1 | First dose | 4 days | sCS, anti-$H_1$, omalizumab | Resolution with no reaction after third booster dose | Female (66%) | 68 | 1 patient with elevated IgE level; 2 patients with positive SARS-CoV-2 spike antibody test results |
| | United States | Moderna | mRNA | 2 | Third dose | 11-12 days | Anti-$H_1$, sCS | Improvement but no resolution | | 24 and 31 | |
| Ben-Fredj et al[28] | Tunisia | Moderna<br>Pfizer-BioNTech<br>AstraZeneca<br>Sinovac/CoronaVAC | mRNA<br>mRNA<br>VV<br>iVV | 2<br>4<br>2<br>2 | First in 8 cases<br>Second in 2 cases | 28.5 days (median) | Anti-$H_1$ | Resolution 2-6 mo later | Female (70%) | 31 (median) | Negative skin prick test results to suspected COVID-19 vaccines as well as vaccine excipients (PEG or PS 80) |
| Castro Silva et al[29] | Brazil | Sinovac/CoronaVAC | iVV | 2 | First dose | 12 weeks and 4 hours | Anti-$H_1$, sCS, omalizumab in 1 patient | Resolution after 9 wk in 1 patient; improvement for the other patient | Female (100%) | 32 and 48 | AID (Hashimoto thyroiditis) history in both patients<br>COVID-19 infection history in 1 patient<br>Asthma and allergic rhinoconjunctivitis history in 1 patient |

*Anti-$H_1$*, $H_1$ antihistamine; *iVV*, inactivated viral vaccine; *PEG*, polyethylene glycol; *PS 80*, Polysorbate 80; *SARS-CoV-2*, severe acute respiratory syndrome coronavirus 2; *sCS*, systemic corticosteroid; *tCS*, topical corticosteroid; *VV*, viral vector.

predominance of middle-aged female patients and mRNA vaccines most frequently implicated (Table III).[20,21,23,24,26,27] Our patients developed CSU after their first or second dose of COVID-19 vaccine, whereas other reports include CSU development after the first, second, and even booster doses of vaccine, with 1 case series of 30 patients who developed CSU only after the third booster dose of the vaccine (Table III).[20,22-26] In the COVAC-CU (Effects of COVID-19 Vaccination on Chronic Urticaria Patients) study, flaring among known patients with CSU was also noted to occur with different doses. Most of our patients had features suggestive of an autoallergic CSU phenotype (elevated total IgE, negative autoantibodies, and normal ESR).

In accordance with other published case series, onset of symptoms post vaccination ranged from a few days to several weeks. CSU causation is complex, involving multiple immune and nonimmune pathways.[2] Despite a growing number of CSU cases on exposure to vaccination, these cases should be considered as an associated rather than necessarily the *de novo* cause of chronic urticaria.

The components of COVID-19 vaccines involved in either triggering new-onset CSU or exacerbating preexisting chronic urticaria remain unknown, but there are several factors to consider. Numerous cutaneous manifestations to severe acute respiratory syndrome coronavirus 2 infection have been reported, most commonly maculopapular- or papulovesicular-type eruptions as well as an unusual phenomenon known as pernio; urticaria was less commonly reported during or after natural infection.[31,32] In contrast, acute urticaria and angioedema have been reported as the most common cutaneous manifestations (after local injection-site reactions) following COVID-19 vaccination.[17,33,34] Furthermore, the mRNA vaccines have been more commonly associated with both acute urticaria and exacerbations of CSU in the COVAC-CU study. These features suggest that it is more likely that vaccine components rather than specifically viral antigens are triggering urticaria post vaccination. Most new-onset CSU cases seem to have an autoallergic rather than autoimmune phenotype (noted commonly among published cases and in those experiencing CSU exacerbations postvaccination). Fortunately, most cases of acute urticaria post vaccination are self-limiting, and it is likely that preexisting genetic or unique immune factors underlie these few cases globally that develop chronic rather than acute urticaria.

Recommendations for any subsequent vaccinations will require shared decision making and be based on a patient-specific risk-benefit analysis, considering the future risk of severe COVID-19, as well as measurement of anti–spike IgG titers.

Cases series are limited in the strength of conclusions that can be made. However, for rare conditions they are important. Although ours is the only UCARE center in the country, and we were able to access information from the regulatory agencies, we cannot be certain that our study has not missed other cases of chronic urticaria developing during the national COVID-19 vaccine rollout. This study also has just provided baseline data, and there is thus need for a further longitudinal study to understand the natural history of chronic urticaria post–COVID-19 vaccination.

## Conclusions

COVID-19 vaccination has proven to be safe and effective for patients living with CSU.[30] In addition, new-onset CSU following COVID-19 vaccination is rare, with a gross estimated incidence of 0.2:1,000,000 doses. Nonetheless, it is important to consider and enquire about any potential immune stimulants during the initial assessment of a patient presenting with CSU. Additional data are required to clearly understand the exact pathophysiology, the risk factors, and the best management of new-onset CSU post–COVID-19 vaccination.

## DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: J. Peter received speaker fees from Novartis and Takeda. The rest of the authors declare that they have no relevant conflicts of interest.

We thank all the patients who participated in the study.

**Clinical implications: New-onset CSU is a rare adverse event following COVID-19 vaccination. This case series contributes to limited global data on this topic while providing a summary of case reports currently available.**

### REFERENCES

1. Kolkhir P, Church MK, Weller K, Metz M, Schmetzer O, Maurer M. Autoimmune chronic spontaneous urticaria: what we know and what we do not know. J Allergy Clin Immunol 2017;139:1772-81.e1.
2. Kolkhir P, Giménez-Arnau AM, Kulthanan K, Peter J, Metz M, Maurer M. Urticaria. Nat Rev Dis Prim 2022;8:61.
3. Gonçalo M, Gimenez-Arnau AM, Al-Ahmad M, Ben-Shoshan M, Bernstein J, Ensina L, et al. The global burden of chronic urticaria for the patient and society. Br J Dermatol 2021;184:226-36.
4. Bracken SJ, Abraham S, MacLeod AS. Autoimmune theories of chronic spontaneous urticaria. Front Immunol 2019;10:1-10.
5. Kanani A, Betschel SD, Warrington R. Urticaria and angioedema. Allergy Asthma Clin Immunol 2018;14:1-13.
6. Grzanka A, Machura E, Mazur B, Misiolek M, Jochem J, Kasperski J, et al. Relationship between vitamin D status and the inflammatory state in patients with chronic spontaneous urticaria. J Inflamm (Lond) 2014;11:1-5.
7. Magen E. Chronic spontaneous urticaria following vaccination. Int J Adv Res 2018;6:1434-9.
8. Worldometers, COVID-19 Coronavirus pandemic. Coronavirus Cases. Available at: https://www.worldometers.info/faq/. Accessed December 7, 2022.
9. Holder J. Tracking Coronavirus vaccinations around the world [Internet]. The New York Times. 2022. Available from: https://www.nytimes.com/interactive/2021/world/covid-vaccinations-tracker.html. Accessed December 7, 2022.
10. Panda M, Dash S, Behera B, Sil A. Dermatological manifestations associated with COVID-19 infection. Indian J Dermatol 2021;66:237-45.
11. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. J Eur Acad Dermatol Venereol 2020;34:e212-3.
12. Galván Casas C, Català A, Carretero Hernández G, Rodríguez-Jiménez P, Fernández-Nieto D, Rodríguez-Villa Lario A, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. Br J Dermatol 2020;183:71-7.
13. Abasaeed Elhag SA, Ibrahim H, Abdelhadi S. Angioedema and urticaria in a COVID-19 patient: a case report and review of the literature. JAAD Case Rep 2020;6:1091-4.
14. Klyucharova A, Martynova E, Rizvanov A, Khaiboullina S. Exacerbation of chronic spontaneous urticaria symptoms in COVID-19 patients, case report. Bionanoscience 2022;12:1482-8.
15. Muntean IA, Pintea I, Bocsan IC, Dobrican CT, Deleanu D. Covid-19 disease leading to chronic spontaneous urticaria exacerbation: a Romanian retrospective study. Healthcare (Basel) 2021;9:1-10.
16. Català A, Muñoz-Santos C, Galván-Casas C, Roncero Riesco M, Revilla Nebreda D, Solá-Truyols A, et al. Cutaneous reactions after SARS-CoV-2 vaccination: a cross-sectional Spanish nationwide study of 405 cases. Br J Dermatol 2022;186:142-52.
17. Peter J, Day C, Takuva S, Takalani A, Engelbrecht I, Garrett N, et al. Allergic reactions to the Ad26.COV2.S vaccine in South Africa. J Allergy Clin Immunol Glob 2022;1:2-8.

18. Mcmahon DE, Amerson E, Rosenbach M, Lipoff JB. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: a registry-based study of 414 cases. Am Acad Dermatol 2021;85:46-55.
19. Latest vaccine statistics. Pretoria, South Africa: Department of Health (Republic of South Africa), 2022. Available at: https://sacoronavirus.co.za/latest-vaccine-statistics/. Accessed December 7, 2022.
20. de Montjoye L, Herman A, Baeck M. Chronic spontaneous urticaria following COVID-19 vaccination. JAAD Case Rep 2022;25:35-8.
21. Magen E, Yakov A, Green I, Israel A, Vinker S, Merzon E. Chronic spontaneous urticaria after BNT162b2 mRNA (Pfizer-BioNTech) vaccination against SARS-CoV-2. Allergy Asthma Proc 2022;43:30-6.
22. Thomas J, Thomas G, Chatim A, Shukla P, Mardiney M. Chronic spontaneous urticaria after COVID-19 vaccine. Cureus 2021;13:9-11.
23. Adame MJ, Christians NA, Mohammed AQ, Tripple JW. Chronic spontaneous urticaria following Pfizer-BioNTech coronavirus disease 2019 messenger RNA vaccination. Ann Intern Med Clin Cases 2022;1:2021-3.
24. Brooks SG, De Jong AM, Abbaslou M, Sussman G. Chronic spontaneous urticaria triggered by the AstraZeneca/Oxford COVID-19 vaccine with achieved remission: a case report. Allergy Rhinol 2022;13:19-20.
25. Suan D, Lee AYS. Chronic spontaneous urticaria following ChAdOx1-S COVID-19 vaccination. Allergo J Int 2022;31:121-2.
26. Pescosolido E, Muller YD, Sabaté-Brescó M, Ferrer M, Yerly D, Caubet JC, et al. Clinical and immunological data from chronic urticaria onset after mRNA SARS-CoV-2 vaccines. Clin Exp Allergy 2022;52:1343-6.
27. Strahan A, Ali R, Freeman EE. Chronic spontaneous urticaria after COVID-19 primary vaccine series and boosters. JAAD Case Rep 2022;25:63-6.
28. Ben-Fredj N, Chahed F, Ben-Fadhel N, Mansour K, Ben-Romdhane H, Mabrouk RS El, et al. Case series of chronic spontaneous urticaria following COVID-19 vaccines: an unusual skin manifestation. Eur J Clin Pharmacol 2022;78:1959-64.
29. Castro Silva R, Castro Silva G, Castro Silva M, Lupi O. Cutaneous reactions following CoronaVac COVID-19 vaccination: a case series of six healthcare workers from a single centre. J Eur Acad Dermatol Venereol 2021;35:e861-4.
30. Purayil S, Thalappil S, Al-Nesf M, Kocaturk E. Chronic urticaria and COVID-19 vaccination: Qatar data (preliminary report of COVAC-CU-international). Qatar Med J 2022;2022:1-2.
31. Seirafianpour F, Sodagar S, Pour Mohammad A, Panahi P, Mozafarpoor S, Almasi S, et al. Cutaneous manifestations and considerations in COVID-19 pandemic: a systematic review. Dermatol Ther 2020;33:e13986.
32. Elmas ÖF, Demirbaş A, Özyurt K, Atasoy M, Türsen Ü. Cutaneous manifestations of COVID-19: a review of the published literature. Dermatol Ther 2020;33:1-5.
33. Anvari S, Samarakoon U, Fu X, Jaggers J, Gonzalez-Estrada A, Chong HJ, et al. Urticaria and/or angioedema events secondary to mRNA COVID-19 vaccinations—updates from a national case registry. J Allergy Clin Immunol 2022;149:AB314.
34. Wolfson AR, Freeman EE, Blumenthal KG. Urticaria 12 days after COVID-19 mRNA booster vaccination. JAMA 2022;327:1702-3.