




Report

Dermatological manifestations associated with COVID-19 and COVID-19 vaccination: results from the Lebanese COVID registry

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Abstract

Background A number of cutaneous manifestations and adverse cutaneous reactions have been associated with COVID-19 infection and vaccine.

Objectives A Lebanese national registry was established to characterize the dermatologic manifestations and adverse cutaneous reactions associated with COVID-19 infection and vaccination in a sample of the Lebanese population.

Methods An observational cross-sectional study was conducted via a web-based clinical form distributed to physicians wishing to report their cases from May 2021 till May 2022.

Results In total, 142 patients were entered in the registry, of which 133 were adults and nine were pediatric patients. The main dermatological manifestations reported with COVID-19 infection in the adult group were urticaria (32.9%), telogen effluvium (21.4%), morbilliform (10%), and papulosquamous (8.6%) eruptions. Urticaria was the most common adverse cutaneous reaction to the vaccine (33%). Interestingly, herpes zoster was triggered in 12 patients post vaccination in our series with this finding more frequently seen in patients above the age of 41 ($P = 0.013$). In the pediatric group, the most reported dermatological findings associated with COVID-19 infection were malar erythema (25%) and telogen effluvium (25%). One 16-year-old patient developed lichen planus after one dose of a COVID-19 vaccine. No deaths were reported in both age groups.

Conclusion This Lebanese registry adds more robust evidence that clinical manifestations of the COVID-19 virus and vaccine are diverse. More studies are necessary to establish the pathophysiology of these dermatological findings in the context of COVID-19 infection and vaccination.

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Conflict of interest: None.

Funding source: This study was funded by the Lebanese American University research grant request number SRRC-R-2020-238.

doi: 10.1111/ijd.16815

Introduction

COVID-19, linked to the infection with SARS-CoV-2, has been associated with a plethora of cutaneous manifestations with a reported prevalence ranging from 0.2 to 20%.^{1–6} Review articles and case series have documented several types of skin lesions including erythematous macules or papules,^{7–10} urticaria,^{6,11} papulosquamous,¹² varicelliform,^{7–9} morbilliform,¹¹ purpuric lesions,⁷ livedo reticularis-like rashes,⁷ retiform purpura,¹³ petechial eruptions,⁷ and pernio-like acro-ischemic lesions.¹⁴ Given that cutaneous manifestations can be the only expression of the disease, it is important to recognize and characterize them.¹⁵ The relationship between disease severity and dermatological manifestations as well as onset and timing of the eruption in the disease course remain unclear.^{16,17} There seems to be a trend linking some types of rashes, such as pernio-like eruption, with an effective antiviral immune response and a better prognosis.¹⁴ Moreover, there have been several adverse cutaneous reactions (ACR) that have been associated with COVID-19 vaccination including local injection site reactions, morbilliform eruptions, urticaria and angioedema as well as delayed local reactions.^{18–21}

Lebanon registered its first case of COVID-19 on February 20, 2020. To date, over 1,200,000 cases have been recorded according to the Lebanese ministry of public health.²² The Lebanese population started receiving the mRNA vaccine, BioNTech, Pfizer vaccine (BNT162b2 mRNA) in February 2021. Probably owing to vaccine hesitancy²³ and lack of proper access to vaccination by the migrant and refugee groups in Lebanon which account for about one-third of the inhabitants, only 35% of the population is estimated to have been completely vaccinated.^{24,25}

In this context, a national Lebanese registry for cutaneous manifestations related to SARS-CoV-2 infection and COVID-19 vaccination was launched in May 2021. We hereby report the results of this national registry to better characterize the cutaneous lesions associated with COVID-19 and COVID-19 vaccination in the Lebanese population.

Materials and methods

An observational cross-sectional study was conducted via a web-based clinical form (www.covidrash-lb.com), which was

electronically completed by physicians wishing to report their cases. The website was sent via email through the participating universities as well as the Lebanese Dermatology Society. Dermatologists as well as physicians working on the frontline, including internists, hospitalists, intensive care unit (ICU) specialists, emergency department (ED) physicians, and family medicine practitioners, were invited to log their cases on the website. Their credentials were verified upon logging onto the website, and data including name, email address, and occupation were recorded. The study was reviewed and approved by the Lebanese American University, Institutional Review Board; IRB #: LAUMCRH.JK1.5/May/2021.

The target population included both adult and pediatric populations. The inclusion criteria were

- Patients with a diagnosis of COVID-19 infection with associated dermatological manifestations as diagnosed by their treating physician. The diagnosis of COVID-19 infection was ascertained by positive SARS-CoV-2 PCR, positive antibody testing, positive antigen testing, or direct contact with laboratory confirmed cases with a suggestive clinical picture.
- Patients with a history of vaccination against COVID-19 with an ACR as diagnosed by their treating physician.

The deadline for case submission was May 2022. Patients' data was deidentified. The patients in this manuscript have given written informed consent to publication of their case details.

Clinical research form

The clinical research form prompted for data pertaining to:

- 1 Demographics of patients, including age, gender, nationality, and country of residence.
- 2 Pertinent preexisting medical conditions including chronic lung disease, diabetes, morbid obesity (BMI 40+), hypertension, cardiovascular disease, chronic kidney disease, cancer, organ transplant recipient, immunodeficiency, inflammatory bowel disease, liver disease, pregnancy, or autoimmune disease or other (to be specified by the physician).

- 3 Presence of preexisting dermatological conditions: psoriasis, pemphigus, cutaneous lupus erythematosus, atopic dermatitis, urticaria, lichen planus, autoimmune bullous disease, or other (to be specified by the physician). Data pertaining to treatments taken for the control of the preexisting dermatological condition were obtained as well.
- 4 COVID-19 illness including: information about diagnosis and testing, date of diagnosis, duration of illness, symptoms of COVID-19, need for hospitalization, need for supplemental oxygen, complications arising from COVID-19, deaths due to COVID-19, and pharmacological treatment of COVID-19.
- 5 COVID-19 vaccine information: type of vaccine received, number of doses taken, date of first vaccination, presence of ACR to first dose, second dose, third dose, or a combination of the latter, history of vaccine allergy, and history of known drug reaction.
- 6 Details concerning dermatological manifestations associated with COVID-19 including the type of dermatological manifestation (cutaneous, mucous membrane, hair or nail changes), classification of the dermatological manifestation as previously reported in the literature,^{26–28} time of onset in relation to COVID-19 symptoms or diagnosis, duration, distribution, and treatment of the condition. A visual aid was provided.
- 7 Characterization of the ACR to the vaccine. A visual aid was provided.

Statistical analysis

All statistical analysis was conducted using the SPSS version 28.0 software. Categorical variables were explored and summarized using frequency and percentage. The summary of the continuous variables was reported using the mean, standard deviation, and confidence intervals.

COVID-19-related dermatological manifestations were grouped to facilitate statistical analysis of the data, based on previously published classifications of COVID-19-related cutaneous rashes.^{26–32} A subgroup analysis was done on COVID-19 rash patients with cutaneous or mucous membrane manifestations without hair and nail manifestations. Cases with missing values were excluded from the analysis.

ACR due to COVID-19 vaccines were grouped as follows to in order to facilitate analysis: (i) injection site reactions/local reactions, (ii) urticaria and angioedema, (iii) morbilliform, diffuse erythema, papulosquamous, pityriasis rosea-like rash, (iv) trigger or exacerbation of inflammatory disease of the skin (psoriasis, atopic dermatitis, lichen planus, bullous pemphigoid, pityriasis lichenoides, erythema multiforme), (v) vasculitic reactions, and (vi) herpes zoster. One case of alopecia areata linked to COVID-19 vaccination was excluded from the analysis. Cases with missing values were excluded from the analysis.

Chi-square or Fisher's exact test was used to check for correlations between types of rashes and hospitalization in both groups, as well as relevant risk factors for developing particular types of COVID-19 manifestations.

Results

Overall, 142 patients were entered in the registry, of which 133 were adults and nine were pediatric patients. A total of 99.3% of cases were reported by dermatologists (141/142) with one case reported by a pediatrician.

In the adult group, 65 patients (48.9%) had dermatological manifestations of COVID-19, while 63 patients (47.4%) had ACRs associated with vaccination, and five cases (3.7%) developed both cutaneous manifestations following vaccination and COVID-19. Most patients (98.6%) were of Lebanese nationality ($n = 131$). Ten out of 26 patients (38.5%) with preexisting dermatological conditions were on treatment. One patient maintained on tofacitinib developed a reaction to the virus, and another patient receiving a TNF alpha inhibitor had a reaction to a COVID-19 vaccine. The demographic data and medical history of adult patients are summarized in Table 1.

Adult patients with COVID-19 infection associated cutaneous manifestations

The diagnosis of COVID-19 was confirmed using a positive SARS-CoV-2 PCR in most of the cases (88.6%; 62/70). The rest of the patients were considered to have contracted COVID-19 following positive antibody testing (2.9%; 2/70), positive antigen testing (1.4%; 1/70), and direct contact with laboratory confirmed cases with a suggestive clinical picture (7.1%; 4/70).

The most common symptoms reported with COVID-19 included fever (47.1%; 33/70), cough (45.7%; 32/70), and myalgia (40%; 28/70). Interestingly, nine patients (12.9%) were asymptomatic aside from the dermatological findings.

Of the 70 patients who contracted COVID-19, four (5.7%) required hospitalization to regular floor; however, none necessitated ICU admission. No complications and no deaths were reported in our series.

The mean days from onset to resolution of COVID-19 symptoms was 16 days, but it ranged from 2 to 30 days.

Dermatological manifestations associated with COVID-19 infection in the adult group

Table 2 summarizes the dermatological manifestations of COVID-19 infection in the adult group, their duration, and the temporal relationship between the onset of the dermatological manifestation and the systemic illness.

The most common dermatological findings associated with COVID-19 were urticarial rash (32.9%; 23/70), telogen effluvium (21.4%; 15/70), morbilliform rash (10%; 7/70), and papulosquamous rash (8.6%; 6/70). In 10 out of 70 patients, 14.3% (Table 2), COVID-19 infection triggered the appearance of an inflammatory skin disease. Two patients known to have psoriasis had a flare-up of their disease post-infection (Table 2), but no de novo cases of psoriasis were registered. Other reported findings are outlined in Table 2.

Table 1 Demographic data and pre-existing medical and dermatological history of 142 patients logged in the registry

Demographic data for all cases, <i>n</i> = 142	
Total number of cases logged (i)	142
Total number of adult patients (age >18 years)	133
Total number of pediatric patients (age <18 years)	8
Distribution of cases in adults	
COVID-19 related dermatological manifestations <i>n</i> (%)	65 (48.9)
Vaccine related dermatological manifestations <i>n</i> (%)	63 (47.4)
Both COVID-19 and vaccine dermatological manifestations <i>n</i> (%)	5 (3.7)
COVID-19 related dermatological manifestations, adult population <i>n</i> = 70	
Gender (%)	
Male	7 (10)
Female	63 (90)
Mean age in years (std deviation)	38.3 (12.7)
Pre-existing medical conditions (%)	
Chronic lung disease	1 (1.4)
Diabetes	1 (1.4)
Hypertension	3 (4.3)
Cancer	2 (2.9)
Inflammatory bowel disease	1 (1.4)
Liver disease	1 (1.4)
Pregnancy	1 (1.4)
Migraine	1 (1.4)
Asthma	1 (1.4)
Thalassemia minor	1 (1.4)
Rheumatic heart disease	1 (1.4)
Anemia	1 (1.4)
Polycythemia vera	1 (1.4)
Dyslipidemia	5 (7.1)
Pre-existing dermatological conditions (%)	
Atopic dermatitis	2 (2.9)
Urticaria	4 (5.7)
PUPP	1 (1.4)
Psoriasis	2 (2.9)
Rosacea	3 (4.3)
Lichen planus	2 (2.9)
Alopecia totalis	1 (1.4)
Latex allergy	2 (1.4)
Acne	3 (1.4)
Unknown	7 (10)
Adverse cutaneous reaction to COVID-19 vaccine, adult population, <i>N</i> = 68	
Gender (%)	
Male	26 (38.2)
Female	42 (61.8)
Mean age (std deviation)	47.2 (19)
Pre-existing medical conditions (%)	
Chronic lung disease	2 (2.9)
Diabetes	7 (10.3)
Hypertension	15 (22.1)
Cardiovascular disease	6 (8.8)
Chronic kidney disease	1 (1.5)
Inflammatory bowel disease	3 (1.5)
Thyroid disease	3 (4.4)
Asthma	1 (1.5)
Osteoporosis	1 (1.5)
Dyslipidemia	7 (10.3)

Table 1 Continued

Allergic rhinitis	1 (1.5)
Celiac disease	1 (1.5)
Benign prostatic hyperplasia	1 (1.5)
Irritable bowel syndrome	1 (1.5)
Pre-existing dermatological conditions (%)	10 (14.7)
Atopic dermatitis	2 (2.9)
Urticaria	3 (4.4)
Psoriasis	3 (4.4)
Vulvar lichen sclerosus	1 (1.5)
Acne	1 (1.5)
Demographic data related to pediatric patients, <i>N</i> = 9	
Gender (%)	
Male	4 (44.4)
Female	5 (55.6)
Mean age (std deviation)	11.1 (6.2)
Distribution of cases	
COVID-19 rash <i>n</i> (%)	8 (88.9)
Vaccine related rash <i>n</i> (%)	1 (11.1)
Pre-existing medical conditions for all cases (%)	
Autoimmune disease	1 (11.1)
Irritable bowel syndrome	1 (11.1)
Allergic rhinitis	1 (11.1)
Epilepsy and multiple sclerosis	1 (11.1)
Pre-existing dermatological conditions for all cases	
Atopic dermatitis	2 (22.2)

A total of 77.1% of patients (54/70) reported that the onset of systemic COVID-19 symptoms preceded onset of their dermatologic changes. Interestingly, nine out of 70 patients (12.9%) had no systemic symptoms associated with COVID-19, and the dermatological manifestations were their only complaint.

On bivariate analysis, one out of four (25%) hospitalized patients had a purpuric/vasculitic rash, which was statistically significant (*P* = 0.05) (Table S1). A correlation between type of rash and risk factors for developing a particular rash could not be established. The results of the bivariate analysis are summarized in Table S1.

Non-dermatologic manifestations related to COVID-19 infection are outlined in Table S3.

Pediatric patients with COVID-19 infection-associated cutaneous manifestations

Nine pediatric patients were recorded in this registry. Demographic data and preexisting conditions are displayed in Table 1. Most patients (eight out of nine; 88.9%) were reported to have developed a cutaneous manifestation associated with COVID-19 infection. One case of ACR to a COVID-19 vaccine was noted. Half of the cases were confirmed via a positive nasal PCR for SARS-CoV-2, whereas the other half were diagnosed after direct contact with laboratory confirmed cases with typical symptomatology.

Similar to the adult group, the most common symptoms were fever (50%; 4/8), cough (50%; 4/8), myalgia (37%; 3/8), and headache (12.5%; 1/8). One patient (12.5%) was asymptomatic.

Table 2 COVID-19 related rash characteristics and classification in adult patients and pediatric patients

Adult patients with COVID-19 virus associated dermatological changes <i>n</i> = 70	
Type of dermatological manifestation associated with COVID-19 (%)	
Skin changes (%)	52 (74.3)
Mucous membranes changes (%)	2 (2.9)
Hair changes (%)	19 (27.1)
Nail changes (%)	2 (2.9)
Temporal relation between onset of systemic symptoms of COVID-19 and onset of dermatological manifestations	
After systemic symptoms (%)	54 (77.1)
Before systemic symptoms (%)	1 (1.4)
Simultaneous onset (%)	6 (8.6)
No systemic symptoms (%)	9 (12.9)
Mean duration of dermatological manifestations of COVID-19 in days (std deviation)	
Skin changes only	27.63 (41.6)
Hair changes only	66 (25.9)
Classification of the dermatological manifestation associated with COVID-19 (%)	
Morbilliform	7 (10)
Urticaria	23 (32.9)
Pernio	2 (2.9)
Macular erythema	2 (2.9)
Vesicular	2 (2.9)
Papulosquamous	5 (7.1)
Petechiae	1 (1.4)
Pityriasis rosea	3 (4.3)
Herpes zoster	2 (2.9)
Sarcoidosis	1 (1.4)
Lichen planus	2 (2.9)
Rosacea	1 (1.4)
Eczema	2 (2.9)
Psoriasis	2 (2.9)
Recurrent oral stomatitis	1 (1.4)
Telogen effluvium (%)	15 (21.4)
Full regrowth of hair in a patient with alopecia totalis (%)	1 (1.4)
Alopecia areata triggered (%)	1 (1.4)
Onychomadesis (%)	2 (2.9)
Hospitalizations (%)	4 (5.7)
Complications (%)	0 (0)
Death (%)	0 (0)
Pediatric patients with COVID-19 virus associated dermatological changes <i>n</i> = 8	
Type of dermatological manifestation associated with COVID-19	
Skin changes	6 (75%)
Hair changes	2 (25%)
Temporal relation between onset of systemic symptoms of COVID-19 and onset of dermatological manifestations	
After systemic symptoms	6 (75%)
Simultaneous onset	1 (12.5%)
No systemic symptoms	1 (12.5%)
Mean duration of dermatological manifestations of COVID-19 in days (std deviation)	
Skin changes	8 (4.8)

Table 2 Continued

Classification of the dermatological manifestation associated with COVID-19 in the pediatric group	
Urticaria	1 (12.5)
Vesicular (%)	1 (12.5)
Pityriasis rosea (%)	1 (12.5)
Pustular (%)	1 (12.5)
Malar erythema (%)	2 (25)
Telogen effluvium (%)	2 (25)
Hospitalizations (%)	0 (0)
Complications (%)	0 (0)
Death (%)	0 (0)

Table 3 Adverse cutaneous reactions (ACRs) occurring post vaccine

Number of patients reporting an ACR secondary to COVID-19 vaccination	
Total number of patients	68
Patients with ACR only	63
Both ACR and COVID-19 rash	5
Patients with two ACRs (to the first and second dose)	10

Distribution and characterization of the ACRs reported

Type of ACR	Number of ACRs reported in 68 patients			
	First dose	Second dose	Third dose	Total number of ACRs (%)
Injection site reaction	3	1	0	4 (5.1)
Morbilliform rash	4	1	0	5 (6.4)
Urticarial rash	10	14	2	26 (33.3)
Herpes zoster	9	2	1	12 (15.4)
Psoriasis (flare)	2	0	0	2 (2.6)
Erythema multiforme	2	1	0	3 (3.8)
Pityriasis rosea	2	1	2	5 (6.4)
Lichen planus (flare)	3	3	0	6 (7.7)
Hard nodule	0	1	0	1 (1.3)
Bullous pemphigoid	0	1	0	1 (1.3)
Vasculitis	0	3	0	3 (3.8)
Papular purpuric gloves and socks syndrome	0	1	0	1 (1.3)
Lichenoid drug eruption	0	1	0	1 (1.3)
Pityriasis lichenoides chronica	0	1	0	1 (1.3)
Ulcers	0	1	0	1 (1.3)
Dishyrotic eczema	0	0	1	1 (1.3)
Angioedema	1	1	0	2 (2.6)
Seborrheic dermatitis	1	1	0	2 (2.6)
Telogen effluvium	0	1	0	1 (1.3)
Total	37	35	6	78 (100)

None of the patients were treated for COVID-19. No hospitalization, no complications, and no deaths were reported among these cases.

The most reported dermatological findings associated with COVID-19 infection were malar erythema (25%; 2/8) and telogen effluvium (25%; 2/8). Table 2 summarizes the findings related to dermatological manifestations of COVID-19 infection in the pediatric group.

Non-dermatologic manifestations related to COVID-19 infection are outlined in Table S3.

Adult patients with ACRs to COVID-19 vaccination

Overall, 78 vaccine related ACRs were reported in 68 adults. The majority (76.5%; 52/68) had received the BioNTech, Pfizer (BNT162b2 mRNA) vaccine. The rest of the patients received the following: AstraZeneca (AZD1222 (ChAdOx1)) (10.3%; 7/68), Sputnik (Gam-COVID-Vac) (5.9%; 4/68), Moderna (mRNA-1273) (1.5%; 1/68), Sinopharm (BBIBP-CorV 1) (1.5%; 1/68), and unknown (4.3%; 3/68).

At the time of the study, 14 patients received only the first dose of a COVID-19 vaccine, 49 patients received the first two doses, and six patients received all three doses.

The cutaneous reactions occurred in 27 patients (39.7%) after the first dose, in 25 patients (36.8%) following administration of the second dose, and in six patients (8.82%) following the third dose. Interestingly, 10 patients (14.7%) experienced an ACR following both first and second doses.

The distribution of the vaccine-related ACRs is presented in Table 3. Vaccination triggered herpes zoster in nine patients (13%) following the first dose, two patients (3%) following the second dose, and one patient (1.5%) following the third dose.

Ten patients (14.7%) were reported to have an ACR to both first and second vaccine doses. They were distributed as follows: urticaria (7%; 5/68), morbilliform (1.5%; 1/68), erythema multiforme (1.5%; 1/68), lichen planus (1.5%; 1/68), seborrheic dermatitis (1.5%; 1/68), and angioedema (1.5%; 1/68).

Two patients known to have psoriasis had a flare-up of their disease post-vaccination (Table 3), but no de novo cases of psoriasis were registered.

On average, the ACR developed within 4 days post-vaccine administration. The most common associated symptoms were fatigue (48.5%; 33/68), fever (23.5%; 16/68), and myalgias (23.5%; 16/68). Seven patients (10.3%) required an ER visit while two (3%) needed hospital admission.

The results of the bivariate analysis are summarized in Table S2. No cases of injection site reaction were recorded in patients aged 41 and more ($P = 0.025$); however, 29% of patients (10/34) above the age of 41 developed herpes zoster following vaccination as compared to 6% of patients (2/33) below the age of 41 ($P = 0.013$). None of the vaccine types correlated with a particular ACR.

Non-dermatologic manifestations related to COVID-19 vaccination are outlined in Table S4.

Pediatric patients with ACRs to COVID-19 vaccination

One 16-year-old girl known to have multiple sclerosis and epilepsy developed lichen planus 21 days after one dose of a COVID-19

(BNT162b2 mRNA) vaccine. She had no complications or hospital admission and no history of drug hypersensitivity.

Discussion

In this Lebanese registry, we report a myriad of cutaneous manifestations likely due to the COVID-19 virus with urticaria, morbilliform, and papulosquamous rashes being the most common in decreasing order. This is in concordance with findings in the Middle East region, specifically in Iraq.^{33,34} In addition, the most common hair manifestation was telogen effluvium which has also been frequently reported across the globe, including in Iran.^{29,30} The mean onset of telogen effluvium post-COVID-19 was around 60 days which is earlier than classic acute telogen effluvium which occurs approximately 3 to 4 months after a triggering event.²⁹

Previous reviews have combined COVID-19-associated rashes into six categories: (i) urticarial rash, (ii) confluent erythematous/maculopapular/morbilliform rash, (iii) papulovesicular exanthem, (iv) chilblain-like acral pattern, (v) livedo reticularis/racemosa-like pattern, and (vi) purpuric “vasculitic” pattern.^{26–28} Most of the patients infected with COVID-19 in association with dermatological findings had no complications related to the disease. This might highlight a favorable prognosis when a person contracts COVID-19 and develops urticaria, morbilliform, or papulosquamous rash. In fact, other reviews have delved into this relationship.^{26,27} Urticarial, confluent erythematous/maculopapular/morbilliform, papulovesicular rashes, and chilblain-like acral pattern were associated with a mild-to-moderate COVID-19 disease severity. In contrast, livedo reticularis/racemosa-like and purpuric “vasculitis” patterns were correlated with a more severe course.^{26,27}

The pathogenesis behind these rashes remains to be clarified, and true causality with the COVID-19 virus has yet to be established. Zhao et al. demonstrated that ACE2-positive keratinocytes were detected in the epidermis, providing a possible explanation for the underlying pathogenesis of COVID-19-mediated cutaneous manifestations.²⁸ Hypotheses have been put forth linking confluent erythematous/maculopapular/morbilliform rashes to virus-specific T cells migrating from circulation into the skin.²⁸ Others have attributed it to direct cytopathic effect of SARS-CoV-2 and cytokine storm.²⁷ As for urticaria, previous studies hypothesized that mast cell degranulation was a result of viral IgM and IgG cross-reacting with mast cell IgE.³⁵ Inflammation caused by SARS-CoV-2 binding to vascular endothelium with thrombosis has been postulated to be responsible for the chilblain-like acral, livedo reticularis/racemosa-like and purpuric “vasculitis” patterns.²⁷ Concerning telogen effluvium, multiple hypotheses have been proposed including elevated levels of interleukin 6 and interferon which inhibit hair matrix cells proliferation.²⁹ Moreover, increased interleukin 1 β and metalloproteinases 1 and 3 levels have been attributed to inhibit hair follicle growth.²⁹

In addition to these previously described dermatological manifestations, patients with preexisting dermatologic conditions can experience a trigger or a flare-up of their primary disease. In fact, this registry reported two cases of psoriasis flare-up post-infection and two others that developed post-vaccination. Dermatologists should be aware of these reactions to be able to provide proper patient education and shed light on appropriate management during the COVID-19 pandemic. A recent review on COVID-19 in patients with atopic dermatitis and chronic spontaneous urticaria revealed that flare-ups are common.³⁶

The advent of COVID-19 vaccines offered a glimpse of hope to fight the pandemic. However, there have been numerous reports of ACRs post-vaccine administration.^{31,37} This registry corroborates these results with a multitude of different skin manifestations with the most common being urticaria and herpes zoster. Urticarial rashes are classified as type I hypersensitivity reactions and thought to be caused by polyethylene glycols (PEGs) and cross-reactive polysorbate 80 found in COVID-19 vaccines.^{31,38} VZV reactivation after COVID-19 vaccination has been massively reported in case series all over the world and even documented in the VAERS of the Centers for Disease Control and Prevention.^{31,32} The Lebanese Ministry of Public Health recently released a pharmacovigilance report with 11 cases of herpes zoster following the Pfizer vaccine.³⁹ The underlying pathogenesis may be the result of an immune reaction process to mRNA vaccines.³² Questions have been raised whether herpes zoster following vaccination is a mere coincidence or a true causality. As a matter of fact, the mass vaccination along with the emphasized scrutiny regarding vaccine safety profile may lead to bias regarding skin manifestations not caused by the COVID-19 vaccination but developed incidentally.³¹ The lower number of vaccine-related manifestations reported in this registry can be attributed to the vaccine reluctance in Lebanon.²³ In comparison to other registries, previous reviews declared unspecific injection-site reactions with the highest frequency post vaccine.³¹ The probable underreporting of these reactions in our registry might be attributed to the fact that these were self-resolving; therefore, patients would not seek medical advice. The underlying mechanism behind these skin phenomena has been linked to the spike protein found in the COVID-19 vaccines.^{31,40} Less common cutaneous reactions have been reported with the vaccine; for instance, El Sayed et al. reported a case of morphea occurring during COVID-19 infection with a reactivation after one dose of a COVID-19 vaccine.⁴¹ More studies are needed to elaborate on the pathogenesis of each reaction pattern. In our registry, 14.7% of our patients developed an ACR following the first two doses of one of a COVID-19 vaccine, which can be interpreted as a hypothetical rechallenge.

At the beginning of the pandemic, the pediatric population was thought to be less affected by COVID-19. With time, more pediatric cases started to emerge. This registry highlights similar

cutaneous manifestations in adults as well as in the pediatric population. Nevertheless, in comparison to the adult population, malar erythema and telogen effluvium were the most frequently reported features of the COVID-19 virus. In contrast to this registry, the literature describes chilblain-like lesions, erythema multiforme, and urticaria as the most common skin features of the COVID-19 virus.^{42,43} To the best of our knowledge, lichen planus following COVID-19 vaccination has only been reported in the adult population.⁴⁴ The registry reveals the first case of lichen planus post vaccination in the pediatric population.

One limitation to this study is the underrepresentation of the refugee population. As a matter of fact, Lebanon is the country with the highest number of refugees per capita.⁴⁵ Lebanon has been traversing an economic crisis during the past 3 years. Moreover, the Beirut port explosion and COVID-19 pandemic accelerated the breakdown of public services. Importantly, Lebanon's healthcare system is primarily driven by private hospitals which offer up to 75% of all healthcare services, while vulnerable patients rely on public institutions. Given that this study was mostly conducted in private tertiary centers, this subset of population is underrepresented in our sample.

A second limitation is the inability to recruit patients who presented to first responders despite our best efforts. Finally, registry fatigue may have contributed to the underreporting of cutaneous findings in first responders who now consider these skin manifestations as classical signs of COVID-19.

A third limitation is the inaptitude to elucidate a causal relationship between these dermatologic manifestations and COVID-19 infection or vaccination or just a concomitance. The literature regarding this matter is still scarce, and more studies that consider these limitations are necessary to confirm our findings.

Conclusion

This Lebanese registry shows that the most common dermatological manifestations reported with COVID-19 are urticaria, telogen effluvium, morbilliform, and papulosquamous eruptions. Urticaria is the most common ACR to the vaccines in our series, and vaccination triggered herpes zoster in 15% of our patients. It is important for dermatologists to recognize these cutaneous manifestations for diagnostic purposes. Moreover, knowledge about these findings allows the dermatologist to provide reassurance while caring for patients. Further research is required to elucidate the pathophysiology behind the cutaneous presentations associated with COVID-19 with their prognostic significance as well as shed light on a possible causality. A better understanding of COVID-19 vaccine-related skin manifestations may be helpful to guide vaccine adoption. Since a clear causal relationship between these cutaneous findings and COVID-19 vaccine has not been established in addition to their low occurrence, patients should not refrain from receiving vaccination.

Acknowledgments

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Bivariate analysis done on COVID-19-associated dermatological manifestations.

Table S2. Bivariate analysis of COVID-19 vaccine associated ACRs. *N* = number of patients with the ACR.

Table S3. Non-dermatologic COVID-19 virus infection symptoms in the adult and pediatric population.

Table S4. Non-dermatologic COVID-19 vaccination symptoms in the adult population.