

Correspondence

Cutaneous manifestations of hospitalized COVID-19 patients in the VIRUS COVID-19 registry

Dear Editor,

In the United States alone, over 65 million cases of COVID-19 have been diagnosed till mid-January 2022, likely underestimating the prevalence as many individuals are asymptomatic and thus untested.¹ Given the global burden and death toll of this pandemic, understanding the presenting signs, disease course, predictors of severity and outcomes, and long-term consequences of COVID-19 is important.

Current literature has documented a vast array of cutaneous manifestations of COVID-19 from maculopapular to vesicular morphology to chilblain-like lesions.² We aimed to assess the prevalence of skin findings, characterization of these presentations, clinical outcomes, and treatment regimens using a multinational database of COVID-19-positive hospitalized patients.

We designed a retrospective observational descriptive study of dermatological symptoms from a large international VIRUS: COVID-19 registry conducted by the Society of Critical Care Medicine (SCCM) Discovery Network. VIRUS is a multinational database that collects and stores patient's data for those who are hospitalized with COVID-19.³ The VIRUS Registry has enrolled hospitalized patients with laboratory confirmed COVID-19 patients. A laboratory confirmed case is defined as a positive result using a reverse-transcriptase-polymerase chain reaction (RT-PCR) assay.

We created data elements based on smaller studies that were published for patients with dermatologic manifestations of COVID-19. We also utilized the expertise of a dermatologist (A.A.) to determine what data points would be valuable to add. The data elements for inclusion were selected to capture the types of skin manifestations that develop, patient demographics, dermatologic comorbidities, existing skin allergies, treatments, and their outcomes. These data elements were used to create an Excel document for collection. To collect dermatological symptoms for each patient, we sent an Excel survey to the sites that recorded patients with "rash" in the database. All sites that mentioned "rash" as a symptom were invited to fill out this Excel form. If sites had noted "urticaria," "hives," "itch," or "mottle" in the Research Electronic Data Capture (REDCap) system, they were also asked to fill out this Excel. The charts were reviewed by research members in each site retrospectively. The data abstractors could review these charts and extract the desired variables. A total of 310 individuals out of the 64,580 patients (0.48%) in the VIRUS COVID-19 registry were reported with skin manifestations. In all, 258 were excluded due to incomplete

information or lack of response from the study site, and the remaining 52 patients were analyzed (Table 1).

Most patients were asymptomatic (32, 61.5%); however, some experienced pain/burning (9, 17.3%) or pruritus (13, 25.0%). Skin manifestations related to COVID-19 varied in morphology. Overall, many patients presented with morbilliform/maculopapular eruptions (26, 50%) (Fig. 1). Exanthems were mainly found on the trunk (29, 55.8%), extremities (26, 50.0%), and face or neck (13, 25.0%). A small number of patients had mucosal involvement (5, 9.6%) or nail involvement (1, 1.9%).

Of the 52 patients in this analysis, 37 were treated with medications. Intravenous antibiotics were provided to 12 (23.1%) patients, and systemic corticosteroids were given to 14 (26.9%)

Table 1 Characteristics of lesions observed in COVID-19 patients and outcomes

	N = (52) (%)
Dermatologic symptoms	
Asymptomatic	32 (61.5)
Pruritus	13 (25.0)
Pain/Burning	9 (17.3)
Comorbid dermatological condition	
Atopic dermatitis	5 (9.6)
Contact dermatitis	2 (3.8)
Psoriasis	2 (3.8)
Stasis dermatitis	1 (1.9)
Quarter of the infection	
April–June 2020	21 (40.1)
July–September 2020	14 (26.9)
October–December 2020	12 (23.1)
January–March 2021	5 (9.6)
Morphology of skin lesion	
Maculopapular/Morbilliform	26 (50.0)
Angioedema/Urticaria	6 (11.5)
Petechial/Purpuric	3 (5.8)
Papulosquamous	3 (5.8)
Erythrodermic	3 (5.8)
Desquamation	1 (1.9)
Hyperpigmentation	1 (1.9)
Livedo reticularis	1 (1.9)
Acneiform	1 (1.9)
Site of involvement	
Trunk	29 (55.8)
Extremities	26 (50.0)
Face/Neck	13 (25.0)
Mucosa	5 (9.6)
Genitals	3 (5.8)
Nail	1 (1.9)



Figure 1 Patient who developed generalized urticarial eruption during active COVID-19 infection

patients. Other common treatments included topical steroids (4, 7.7%) and intravenous immunoglobulins (3, 5.8%).


Several studies have reported cutaneous lesions in patients with COVID-19. Maculopapular and morbilliform lesions are frequently reported among patients.⁴ A majority of these lesions have been reported being on the trunk, with patients typically reporting no symptoms.⁵ This is similarly reported in our study. Some individuals have reported urticarial lesions with angioedema, which are typically pruritic.⁴ Less frequently reported lesions include petechiae and chilblain-like lesions, with livedoid eruptions being reported the least often.⁴ These lesions typically follow a benign course.^{4,5} The mortality rate associated with patients with cutaneous presentations is reported as lower than 5%.⁶

The pathogenesis of cutaneous lesions is still unclear at this time; however, some theories have been postulated. Complement-mediated activation of lymphocytes can lead to release of proinflammatory cytokines, known as “cytokine storm.”⁴ These proinflammatory cytokines, such as IL-6 and tumor necrosis factor alpha (TNF- α), can lead to development of microthrombotic events and vasculopathies that result in livedo-reticularis lesions.⁵ Additionally, COVID-19 is known to enter cells via the angiotensin-converting enzyme 2 (ACE-2) receptor, which is


found in endothelial cells.⁵ It is postulated that the virus can gain entry via this route and lead to cutaneous presentations in patients.⁵

There are a few limitations to our study. Our data were collected retrospectively after sites had already entered their non-dermatological clinical data, so there is a lack in longitudinal collection of data points. Additionally, there may be bias when interpreting the results due to missing data from sites that did not respond.


More than 322 million COVID-19 cases have been reported all over the world by mid-January 2022. Although several hypotheses of the pathophysiological mechanisms of cutaneous lesions have been postulated, it is still unclear how these lesions form. The VIRUS COVID-19 Registry has helped delineate the morphological characteristics and symptomatology of these lesions. Physicians should be aware of the types of lesions that can form to support early diagnosis of COVID-19. Further research can include biopsy of these lesions to better understand the pathophysiology of the cutaneous manifestations.

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