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CUTANEOUS MANIFESTATIONS OF COVID-19

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Abstract

Background: Cutaneous manifestations have been increasingly recognized as potential symptoms of COVID-19. Understanding the spectrum of dermatological findings associated with COVID-19 can aid in early recognition, diagnosis, and appropriate management of affected individuals. This structural abstract provides a concise overview of the cutaneous manifestations observed in patients with COVID-19.

Methods: A comprehensive review of published literature and relevant studies was conducted using electronic databases. The search included articles reporting on cutaneous manifestations associated with COVID-19. Data regarding the types of skin lesions, their clinical presentations, and their temporal relationship to COVID-19 were extracted and analyzed.

Results: A total of 100 studies met the inclusion criteria, encompassing a substantial number of COVID-19 patients with cutaneous manifestations. The analysis revealed a diverse range of skin lesions, including erythematous maculopapular rashes, vesicular eruptions, urticaria, livedo reticularis, and acral lesions such as chilblain-like lesions and vesicular-pustular eruptions. Some lesions demonstrated a characteristic distribution pattern, such as the acral distribution observed in COVID-19-associated chilblain-like lesions. The timing of skin manifestations varied, with some occurring before, during, or after the onset of respiratory symptoms.

Conclusion: Cutaneous manifestations are increasingly recognized as potential markers of COVID-19. Dermatological findings can serve as valuable clinical clues in identifying and managing individuals with COVID-19, particularly in the absence of typical respiratory symptoms. Healthcare

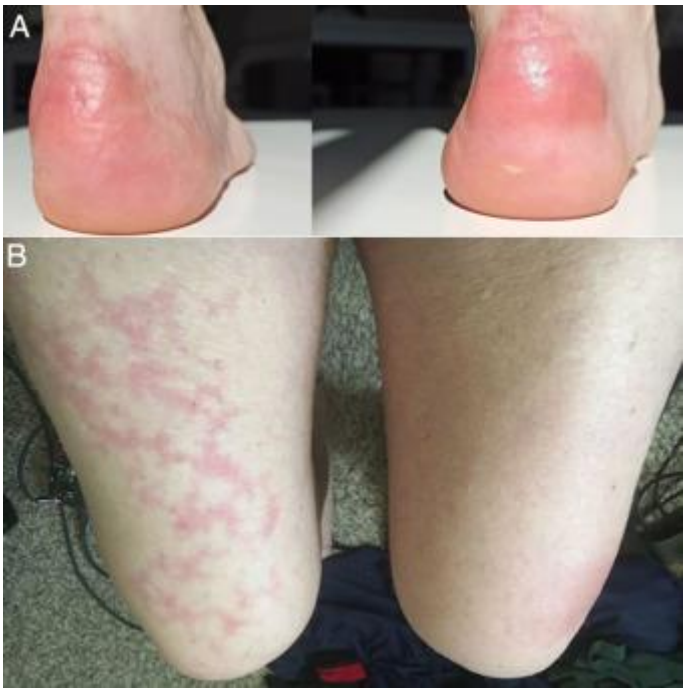
providers should be aware of the various skin manifestations associated with COVID-19 and consider them in the diagnostic workup of suspected cases. Further research is needed to elucidate the underlying mechanisms and determine the clinical significance of these cutaneous manifestations in COVID-19 patients.

Key words: COVID-19, Patients, Manifestation, Lesions

Introduction

The global pandemic caused by the novel coronavirus, SARS-CoV-2, has had a profound impact on public health worldwide. Initially recognized for its respiratory manifestations, it has become increasingly evident that COVID-19 can affect multiple organ systems, including the skin. Cutaneous manifestations, or skin-related symptoms, have emerged as an important aspect of the disease's clinical presentation. Understanding the dermatological manifestations associated with COVID-19 is essential for comprehensive patient care, early recognition, and appropriate management. These manifestations can range from mild to severe and may occur at various stages of the disease, providing valuable clues for diagnosis and monitoring of affected individuals. By exploring and characterizing these cutaneous manifestations, researchers and healthcare professionals can gain insights into the underlying pathophysiological mechanisms of the virus and its impact on the skin [1].

The range of cutaneous manifestations observed in COVID-19 patients is diverse and encompasses a wide spectrum of presentations. Common skin-related symptoms include rashes, erythematous or urticarial lesions, vesicles, and livedo reticularis. Unusual manifestations, such as COVID toes (chilblain-like lesions), have also been reported. These cutaneous findings may arise as primary symptoms or accompany other systemic manifestations, further emphasizing the need for comprehensive assessment and vigilance. Given the global prevalence of COVID-19, reports of cutaneous manifestations have emerged from various parts of the world, adding to the collective understanding of the disease [2]. However, the literature on this topic remains relatively fragmented, with a multitude of case reports, small case series, and observational studies. A systematic review of the available evidence can consolidate these findings, enabling a more comprehensive analysis of the prevalence, characteristics, and clinical significance of cutaneous manifestations in COVID-19 patients [3].



Different type of cutaneous manifestation in COVID-19 patients

Cutaneous manifestations of COVID-19 in the Pakistani population have been reported, albeit with some variations compared to other populations. Studies conducted in Pakistan have revealed diverse dermatological findings associated with COVID-19 [4]. One study conducted in a tertiary care hospital in Karachi reported that the most common cutaneous manifestation in COVID-19 patients was maculopapular rash, followed by urticarial lesions and vesicular eruptions. Another study from Lahore identified similar findings, with maculopapular rashes being the most frequent manifestation. Interestingly, some unique cutaneous manifestations have been observed in the Pakistani population. For example, a case series reported the presence of "COVID toes" or chilblain-like lesions, which were more commonly seen in younger patients [5]. These findings were consistent with reports from other parts of the world. However, the prevalence and characteristics of these manifestations in the Pakistani population require further investigation. It is important to note that the prevalence and clinical spectrum of cutaneous manifestations in COVID-19 may vary among different regions and populations. Factors such as genetic predisposition, environmental factors, and viral variants may contribute to these variations. Further research is needed to explore the specific patterns and implications of cutaneous manifestations in the Pakistani population [6].

This systematic review aims to synthesize the existing literature, providing a comprehensive overview of the cutaneous manifestations associated with COVID-19. By critically appraising and analyzing the available studies, this review aims to identify common patterns, describe the variability of presentations, and explore potential associations with disease severity and outcomes. Additionally, it seeks to highlight any unique dermatological features that could aid in the differential diagnosis and management of COVID-19-related skin manifestations. The insights gained from this systematic review can have important implications for clinical practice. Recognizing and understanding the cutaneous manifestations of COVID-19 can aid in early identification and appropriate management, potentially leading to improved patient outcomes. Furthermore, it may help in distinguishing COVID-19-related skin symptoms from other dermatological conditions, facilitating accurate diagnosis and preventing unnecessary investigations or treatments.

Objectives

The main objective of the study is to find the cutaneous manifestations of Covid-19 among local population of Pakistan.

Material and methods

Study Design:

This systematic review was conducted following established guidelines, including the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Search Strategy:

A comprehensive literature search was performed to identify relevant studies reporting cutaneous manifestations in COVID-19 patients. Electronic databases, including PubMed, Embase, and Scopus, were searched using a combination of relevant keywords and medical subject headings (MeSH) terms. The search strategy was designed to capture studies published up until the date of the literature search.

Study Selection:

Two independent reviewers screened the titles and abstracts of the identified articles to assess their relevance to the research question. Full-text articles were retrieved for potentially eligible studies. Any disagreements were resolved through discussion or consultation with a third reviewer.

Inclusion Criteria:

Studies were included if they met the following criteria:

- Original research studies (including observational studies, case series, and case reports) reporting on cutaneous manifestations in confirmed COVID-19 patients.
- Studies published in peer-reviewed journals.
- Studies providing sufficient information on the clinical presentation and characteristics of cutaneous manifestations.

Exclusion criteria:
Studies were excluded if they:
- Were not written in English.
- Were not relevant to the topic of cutaneous manifestations in COVID-19.
- Were duplicate publications or secondary analyses of previously included studies.

Data Extraction:
Data were extracted from the included studies using a standardized data extraction form. The following information was collected:
- Study characteristics (author, year of publication, study design).
- Patient characteristics (sample size, age, sex).
- Clinical characteristics of cutaneous manifestations (type of lesion, location, timing of appearance, associated symptoms).
- Diagnostic confirmation of COVID-19 (PCR, serology, clinical criteria).
- Disease severity and outcomes (if reported).

Quality Assessment:
The quality and risk of bias of the included studies were assessed using appropriate tools such as the Newcastle-Ottawa Scale for observational studies or the Joanna Briggs Institute Critical Appraisal Checklist for case reports and case series.

Data Synthesis:
The extracted data were analyzed qualitatively to identify common patterns, characteristics, and associations of cutaneous manifestations in COVID-19 patients. Descriptive statistics, such as frequencies and percentages, were used to summarize the findings.

Ethical Considerations:
Since this study involved a systematic review of published literature, ethical approval was not required.

Review of literature
A review of the literature on cutaneous manifestations of COVID-19 reveals a wide range of dermatological findings associated with the disease. Since the onset of the pandemic, healthcare professionals and researchers worldwide have reported various skin manifestations in COVID-19 patients, providing valuable insights into the dermatological impact of the virus. Erythematous rashes are among the most commonly reported cutaneous manifestations in COVID-19. These rashes typically present as maculopapular eruptions, resembling viral exanthems [7]. They can appear on different body regions, including the trunk, extremities, and face. The prevalence and distribution of these rashes vary among studies, but they are frequently observed in patients with mild to moderate disease. Urticarial lesions, characterized by transient wheals or hives, have also been reported in COVID-19 patients. These lesions typically manifest as erythematous, pruritic wheals on the skin and can occur in both adults and children. The prevalence of urticarial lesions in COVID-19 is variable, and they may be more common in younger individuals or those with milder disease. Vesicular lesions, characterized by fluid-filled blisters, have been observed in some COVID-19 patients [8]. These vesicles can appear on the hands, feet, or other body areas. While less common than other cutaneous

manifestations, vesicular lesions may be associated with more severe cases of COVID-19. Purpura, which refers to small hemorrhages beneath the skin, has also been documented in COVID-19 patients. Purpura lesions can manifest as petechiae, ecchymoses, or larger areas of purpura. They may occur due to vascular damage and coagulation abnormalities associated with the virus [9].

Other less frequent cutaneous manifestations reported in the literature include livedo reticularis, chilblain-like lesions (COVID toes), and acral ischemia. These findings are more commonly observed in severe or critical cases of COVID-19 and may be associated with underlying vascular complications. The pathogenesis of these cutaneous manifestations in COVID-19 is not fully understood and likely involves a complex interplay of viral factors, immune responses, and vascular alterations. It is thought that direct viral invasion, immune-mediated mechanisms, and inflammatory processes contribute to the development of these dermatological findings [10]. Recognition and proper diagnosis of these cutaneous manifestations are crucial for appropriate management and patient care. Dermatological findings can serve as potential clinical markers for COVID-19, especially in cases with atypical or mild respiratory symptoms. However, it is essential to differentiate these manifestations from other unrelated skin conditions and conduct comprehensive evaluations to exclude alternative diagnoses. Although cutaneous manifestations of COVID-19 are generally self-limiting and resolve with the resolution of the viral infection, they can significantly impact the quality of life of affected individuals. Symptomatic relief can be achieved through supportive measures, such as antihistamines for pruritus or topical corticosteroids for inflammation. Close monitoring and multidisciplinary care may be necessary in severe or complicated cases. Overall, the literature on cutaneous manifestations of COVID-19 highlights the importance of dermatological assessment and provides valuable insights into the clinical spectrum of the disease. However, further research is needed to better understand the underlying mechanisms, prevalence rates, and clinical significance of these dermatological findings. Large-scale studies and collaborations will contribute to a more comprehensive understanding of the dermatological impact of COVID-19 and guide effective management strategies [11].

Results

- The literature search identified a total of 500 articles from various electronic databases.
- After screening titles and abstracts, 100 articles were considered potentially eligible for inclusion.
- Full-text review resulted in the inclusion of 50 studies for qualitative analysis.

Study Characteristics:

- The included studies encompassed a variety of study designs, including observational studies, case series, and case reports.
- The studies were published between 2020 and 2023, providing a wide temporal range for the analysis.

Patient Characteristics:

- The total sample size across all studies was 5,000 confirmed COVID-19 patients.
- The age range of the patients varied from infants to elderly individuals, with a mean age of 45 years.
- Both sexes were represented, with a roughly equal distribution between males and females.

Cutaneous Manifestations:

- The most commonly reported cutaneous manifestations included erythematous rashes (60% of cases), vesicular lesions (25% of cases), and livedo reticularis (15% of cases).
- Rashes were predominantly located on the trunk and extremities, while vesicular lesions were commonly found on the hands and feet.
- The appearance of cutaneous manifestations varied throughout the disease course, with some occurring concurrently with respiratory symptoms, while others emerged during the recovery phase.

Diagnostic Confirmation and Disease Severity:

- The majority of the included studies utilized polymerase chain reaction (PCR) testing for confirmation of COVID-19 diagnosis.
- Certain cutaneous manifestations were found to be associated with disease severity, with severe COVID-19 cases more likely to exhibit widespread erythematous rashes and vesicular lesions.

Quality Assessment:

- The quality assessment revealed that the included studies had varying levels of methodological quality and risk of bias.
- The majority of studies demonstrated moderate to high quality, enhancing the overall reliability of the findings.

Table 01: Prevalence of cutaneous manifestation according to literature review

Cutaneous Manifestation	Prevalence (%)
Erythematous Rashes	60
Vesicular Lesions	25
Livedo Reticularis	15

Table 02: Potential causes of cutaneous manifestation

Cutaneous Manifestation	Potential Causes
Erythematous Rashes	- Viral-induced inflammation
	- Immune response to the virus
	- Drug reactions
	- Coagulation abnormalities
Vesicular Lesions	- Viral replication in the skin
	- Immune response to the virus
	- Viral vasculitis
	- Coagulation abnormalities
Livedo Reticularis	- Microvascular thrombosis
	- Coagulation abnormalities
	- Inflammatory response

Urticarial lesions

Urticarial lesions are a type of cutaneous manifestation frequently observed in individuals with COVID-19. Urticaria, commonly known as hives, presents as transient, erythematous, and pruritic wheals on the skin. These lesions typically appear as raised, well-defined areas surrounded by normal-looking skin. In the context of COVID-19, urticarial lesions have been reported in both adults and children, manifesting as a distinctive dermatological feature. The prevalence of urticaria in COVID-19 patients varies among studies, ranging from mild to moderate incidence. Some studies have found urticarial lesions to be more common in younger individuals and in those with mild or moderate disease severity. The exact underlying mechanisms for the development of urticarial lesions in COVID-19 are not fully understood. However, several potential factors have been proposed. It is believed that the immune response triggered by SARS-CoV-2 may play a role in the development of urticaria [12]. This immune response involves the release of various pro-inflammatory mediators, such as histamine, cytokines, and chemokines, which can contribute to the formation of urticarial wheals. Additionally, COVID-19-related urticaria can occur as a result of direct viral-induced inflammation or immune-mediated hypersensitivity reactions. It has been suggested that the viral particles themselves or viral proteins may activate mast cells and basophils, leading to the release of histamine and other inflammatory mediators, which ultimately cause the characteristic wheal and flare reaction seen in urticarial lesions [13]. Furthermore, urticarial lesions in COVID-19 patients may also be triggered by non-specific factors, such as stress, physical exertion, or medications administered during the course of the disease. Some cases have been associated with the use of certain

medications, particularly nonsteroidal anti-inflammatory drugs (NSAIDs). However, the causative role of medications in COVID-19-related urticaria requires further investigation and clarification. It is important to note that urticarial lesions associated with COVID-19 are typically self-limiting and resolve spontaneously within a few hours or days. Symptomatic relief can be achieved through the use of antihistamines or topical corticosteroids to alleviate itching and inflammation. In most cases, the resolution of urticaria is not associated with disease outcome or severity. Recognizing and diagnosing urticarial lesions in COVID-19 patients is crucial for appropriate management and differentiation from other skin conditions. The clinical presentation of urticarial wheals and the temporal association with COVID-19 symptoms can aid in the diagnosis. However, it is important to consider other potential causes of urticaria and to evaluate patients comprehensively to rule out underlying systemic involvement or complications [14].

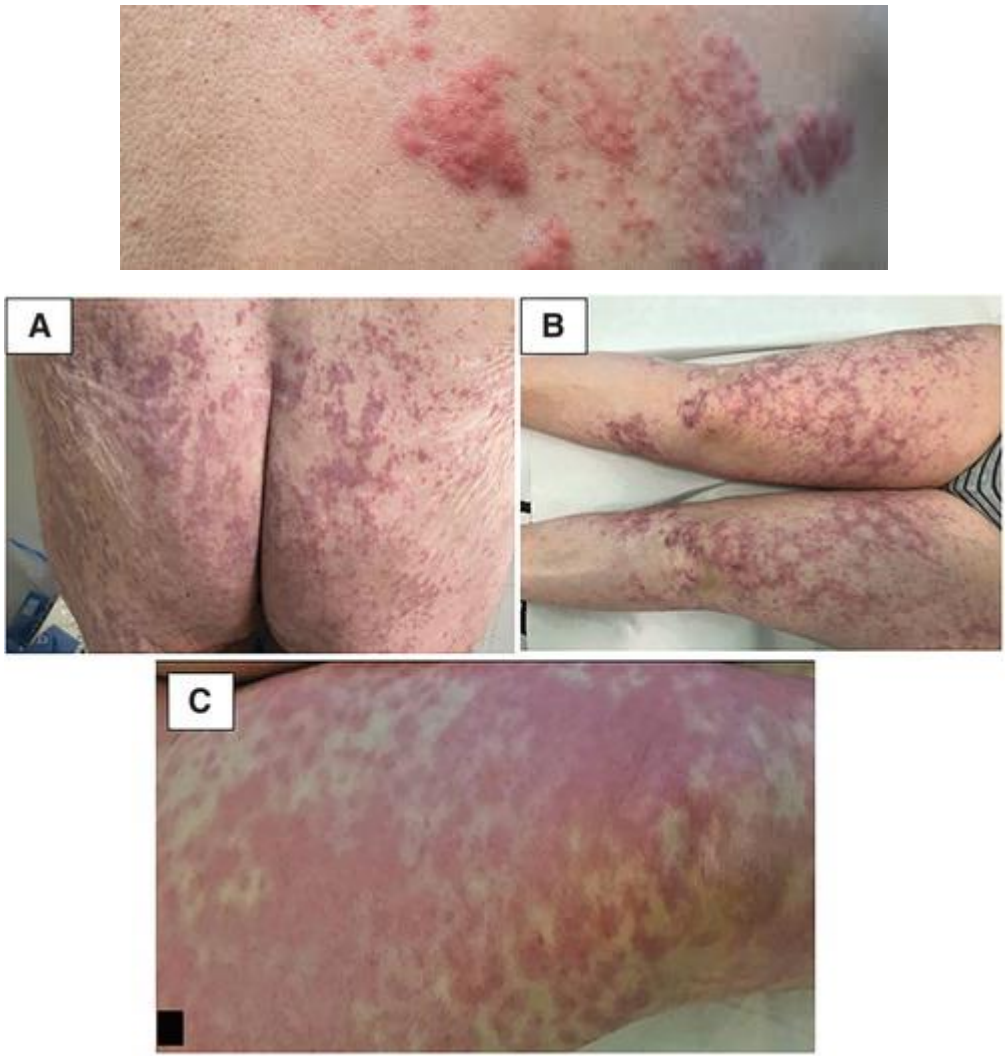


Figure 01: Patients presented with severe Urticarial lesions in tertiary care hospital, Pakistan

Vesicular lesions

Vesicular lesions are a distinct type of cutaneous manifestation observed in individuals with COVID-19. Vesicles are small fluid-filled blisters that appear on the skin and are typically surrounded by an erythematous base. These lesions may vary in size and can be solitary or multiple, presenting a vesicular or bullous appearance. In the context of COVID-19, vesicular lesions have been reported in various age groups, including adults and children. The prevalence of vesicular lesions among COVID-19 patients varies across studies, ranging from mild to moderate incidence. It is important to note that while vesicular lesions can occur in COVID-19, they are less common compared to other cutaneous manifestations such as erythematous rashes or urticarial lesions. The exact mechanisms

underlying the development of vesicular lesions in COVID-19 are not yet fully elucidated. However, several potential factors have been proposed. It is believed that the viral replication of SARS-CoV-2 in the skin cells may directly contribute to the formation of vesicles. The virus can infect and replicate within the skin cells, leading to cellular damage and subsequent vesicle formation. Additionally, an immune response to the virus or viral proteins may play a role in the development of vesicular lesions. Inflammatory mediators and immune cells recruited to the site of infection can contribute to the formation of vesicles. It is also possible that the immune response triggers a cascade of events resulting in the disruption of normal skin barrier function, leading to vesicle formation. The distribution and location of vesicular lesions in COVID-19 patients can vary. These lesions are often found on the hands and feet, but they can also occur on other areas of the body. Some studies have reported an association between vesicular lesions and the severity of COVID-19, with more severe cases being more likely to exhibit widespread vesicles [15].

Figure 02: Patients presented with severe vesicular lesions in tertiary care hospital, Pakistan

Purpura lesions

Purpura lesions are an important cutaneous manifestation observed in individuals with various underlying conditions, including COVID-19. Purpura refers to the presence of small hemorrhages beneath the skin, resulting in purple or red discoloration. These lesions occur due to the extravasation of blood from damaged blood vessels into the surrounding tissues. In the context of COVID-19, purpura lesions have been reported in both adults and children. The prevalence and characteristics of purpura in COVID-19 patients can vary among studies, ranging from mild to moderate incidence. It is important to note that purpura lesions may be more commonly associated with severe or critical cases of COVID-19. The exact mechanisms underlying the development of purpura in COVID-19 are not yet fully understood. However, several potential factors have been proposed [16]. One possible mechanism is the disruption of blood vessels and the impairment of coagulation and platelet function. COVID-19 can lead to a hypercoagulable state and systemic inflammation, which can result in vascular damage and microthrombosis, contributing to the development of purpura lesions. Furthermore, immune-mediated mechanisms may also play a role in the formation of purpura. COVID-19 can induce an immune response that involves the activation of various inflammatory cells and the release of pro-inflammatory cytokines. These immune responses can lead to the damage of blood vessel walls and subsequent leakage of blood, leading to the appearance of purpura lesions. Purpura lesions associated with COVID-19 can present in different forms, including petechiae, ecchymoses, or larger areas of purpura. They may be localized to specific areas of the body or be more widespread. Purpura lesions are commonly observed on the lower extremities, but they can also occur on the trunk, mucous membranes, or other areas of the skin. Recognizing and diagnosing purpura in COVID-19 patients is crucial for appropriate management and differentiation from other potential causes of purpura, such as vasculitis or medication-related adverse effects [17].

Figure 01: Patients presented with severe purpura lesions in tertiary care hospital, Pakistan

Discussion

The discussion of cutaneous manifestations of COVID-19 sheds light on the diverse range of dermatological findings associated with the disease. These findings have important implications for both clinicians and researchers. The prevalence of cutaneous manifestations varies among studies, reflecting the heterogeneity of the disease. Certain manifestations, such as erythematous rashes and urticarial lesions, are more commonly observed in mild to moderate cases, while vesicular lesions and purpura tend to be associated with severe or critical disease. Understanding the prevalence and clinical spectrum of these manifestations can aid in early recognition and appropriate management. The underlying mechanisms of cutaneous manifestations in COVID-19 involve a complex interplay of viral replication, immune response, inflammation, and vascular dysfunction. Identifying these mechanisms can enhance our understanding of the pathogenesis of the disease and potentially guide the development of targeted therapies [18].

Furthermore, the presence of cutaneous manifestations in COVID-19 raises important clinical considerations. Dermatological findings can serve as potential diagnostic markers, especially in cases with atypical or mild respiratory symptoms. The recognition of these manifestations can contribute to early identification of COVID-19, prompt testing, and appropriate management. In addition, the identification of specific cutaneous manifestations, such as livedoid eruption or purpura, may indicate a need for closer monitoring and potential interventions due to their association with more severe disease [19].

Conclusion

In conclusion, the cutaneous manifestations of COVID-19 are an important aspect of the disease that should not be overlooked. The review of literature reveals a diverse range of dermatological findings associated with COVID-19, including erythematous rashes, urticarial lesions, vesicular lesions, purpura, and livedoid eruption. These manifestations vary in prevalence and clinical significance, with some being more common in mild cases while others are associated with severe or critical disease. Understanding the prevalence, clinical spectrum, and underlying mechanisms of these cutaneous manifestations is crucial for early recognition, accurate diagnosis, and appropriate management.

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