SKIN MANIFESTATIONS AND COVID-19 INFECTION: A BIBLIOMETRIC ANALYSIS OF 50 MOST CITED ARTICLES

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Summary

With the onset of the COVID-19 pandemic, numerous cases of various skin manifestations associated with the disease were reported. Given the importance and prevalence of skin manifestations, a bibliometric analysis was conducted to evaluate the landscape of scientific research related to the dermatological manifestations of COVID-19.

Objective: *This study aims to analyze the 50 most cited articles published between the years 2021- 2023 on skin manifestations related to COVID-19.*

Methods: *A systematic search was conducted in the Scopus, PubMed and Medline database using keywords such as "COVID-19," "skin manifestations," and "dermatology."*

Results: *After conducting the search, a total of 1740 articles were listed, of which only 1337 belonged to the period 2021-2023. From these, we identified only the 50 most cited articles necessary for our analysis. 40 articles were written in 2021, accounting for about 80% of the total. Nine articles were written in 2022 (18%), and only one article, was written in 2023. 36% of papers, had a primary focus on the pathophysiology and 86% of them focused on the clinical characteristics and diagnosis*

Conclusion: *This study provides a comprehensive analysis of the scientific research on the dermatological manifestations of COVID-19 and assesses the impact of this research on the field of medicine and its future. The findings are significant not only for better understanding the implications of COVID-19 on the skin but also for aiding in the preparation for similar diseases and guiding future scientific research efforts.*

Keywords: *COVID-19, skin, dermatology, chilblain-like lesions, urticaria, alopecia.*

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Introduction

On March 11, 2020, the World Health Organization (WHO) declared the new coronavirus disease (COVID-19) a global pandemic. While respiratory symptoms and systemic effects have been the primary focus of research, dermatological manifestations have also emerged as significant indicators of the disease. Given that angiotensin-converting enzyme 2 (ACE2) is a crucial functional receptor of SARS-CoV-2, exploration of the ACE2 expression in skin tissues could facilitate to clarify the mechanisms involved in cutaneous manifestations of COVID-19. Various viewpoints about the mechanisms inducing the skin rash in COVID-19 patients have been proposed. Dermatological manifestations associated with COVID-19 have ranged from mild, self-limiting conditions to severe and potentially life-threatening symptoms. Skin manifestations related to SARS-CoV-2 infection can be divided mainly into five groups: chilblain-like lesions (CBLLs), maculopapular

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eruptions, urticarial eruptions, vesicular eruptions, and livedo or necrosis. Other skin findings reported are erythema multiforme (EM)-like lesions and skin findings associated with multisystem inflammatory syndrome in children (MIS-C) and rarely with multisystem inflammatory syndrome in adults (MIS-A). Other manifestations such as pityriasis rosea or shingles are also reported. Understanding the patterns, prevalence, and significance of these skin manifestations is crucial for both dermatologists and other clinicians in recognizing the systemic nature of COVID-19 and its effects on the skin. In the evolving research landscape, a bibliometric analysis of the most cited articles provides a quantitative and qualitative overview of the most influential studies, helping to map research trends and identify leading contributors.

This study aims to review the 50 most cited articles published between 2021 and 2023 on the topic of skin manifestations related to COVID-19, as indexed in Scopus, PubMed and Medline databases. The analysis will explore citation trends, research themes, and key findings to present a comprehensive picture of the current state of knowledge in this field. Such an analysis will offer valuable insights for researchers and healthcare professionals by highlighting important research contributions and potential gaps in the literature.

Material and Method

The bibliometric analysis of the most cited articles was conducted over a time frame from January 2021 to December 31, 2023, using all articles published in Scopus, PubMed and

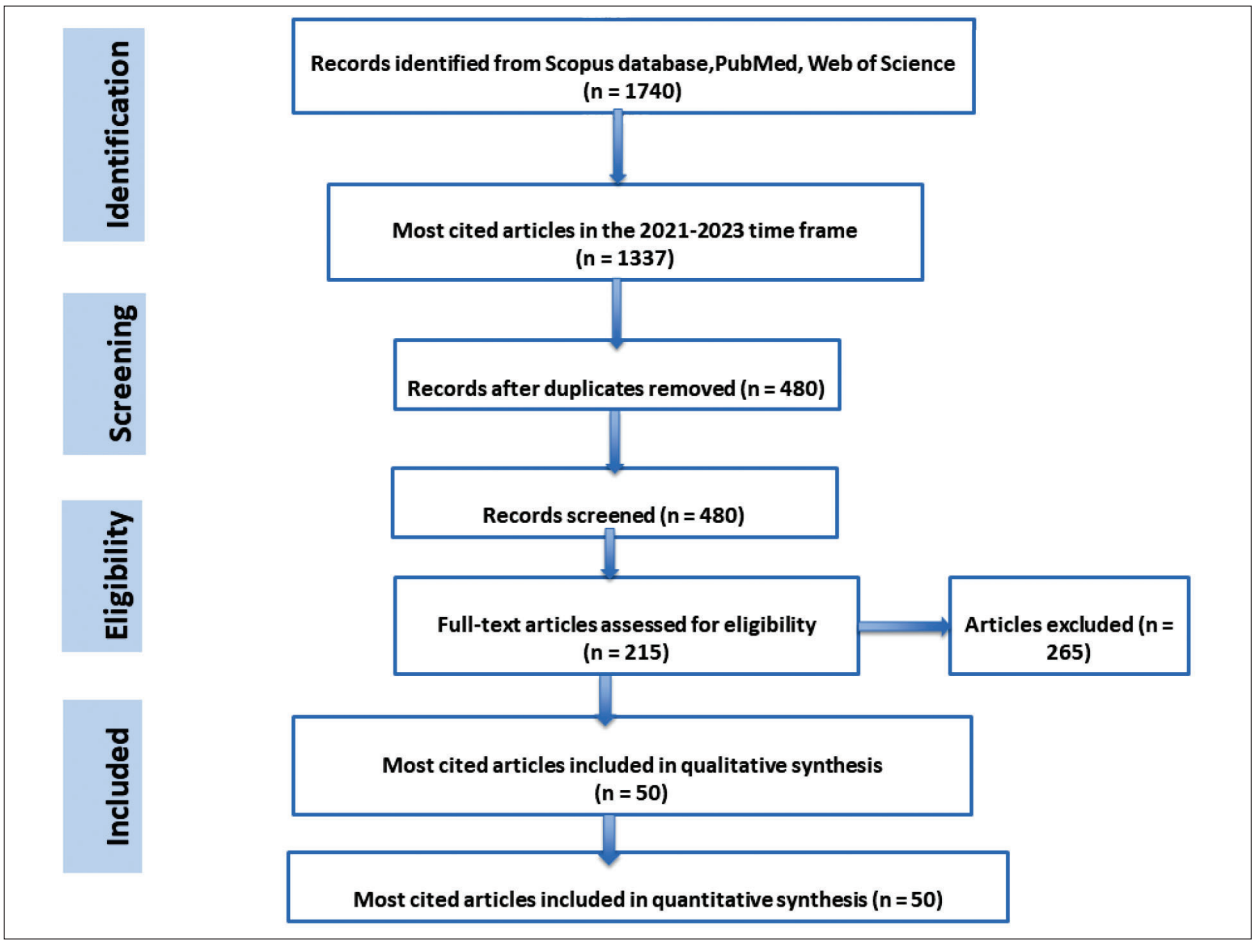

Figure 1. The PRISMA diagram statement of this bibliometric analysis.

Medline databases. The terms used to search for the articles were combined as follows: ("skin manifestations" OR "skin diseases" OR "dermatology" OR "cutaneous signs" OR "dermatologic symptoms" OR "cutaneous symptoms" OR "skin lesions" OR "cutaneous manifestations" OR "dermatologic manifestations" OR "rash" OR "urticaria" OR "erythema" OR "chilblains" OR "COVID toes" OR "urticaria" OR "vesicles" OR "livedo reticularis" OR "petechiae") AND ("COVID-19" OR "COVID19" OR "SARS-COV-2" OR "SARSCOV2" OR "SARS 2" OR "Novel coronavirus" OR "2019-nCov" OR "Coronavirus").

Results

A total of 1740 articles were listed, of which only 1337 belonged to the study period time frame. From these, we identified only the 50 most cited papers necessary for our analysis. All articles analyzed in the bibliometric study were open-access articles.

Out of a total of 50 articles included in our study, 40 (80%) articles were written in 2021, 9 (18%), were written in 2022 and only one (2%) was written in 2023.

According to the analysis, the journals with the most frequent publications were: *The Journal of the European Academy of Dermatology and Venereology* with 5 publications (10%), *JAMA Dermatology* with 3 publications (6%), and the *Journal of the American Academy of Dermatology* with 3 publications (6%), folloued by the *Lancet Infectious Diseases*, *Journal of Clinical Medicine*, *Nature Medicine*, and the *British Journal of Dermatology*, each with 2 publications (4%). The remaining journals account for 31 publications, which makes up 62%.

The most cited articles studied in our analysis were distributed as follows: 9 articles (18%) were case reports, 9 (18%) were clinical trials, 5 (10%)

Table 1. Top 50 most cited articles about skin manifestations and Covid-19

	TITLE OF PAPER	AUTHORS	JOURNAL	YEAR	NR. OF CITATIONS
1	Post-acute COVID-19 syndrome	A.Nalbandian. et.al Academy of Dermatology and Venereology	*Journal of the European*	2021	2794 (4)
2	High-dimensional characterization of post-acute sequelae of COVID-19	Z. Al-Aly et.al	*The Lancet Infectious Diseases*	2021	871 (5)
3	Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: A registry-based study of 414 cases	Devon E. McMahon et.al	*International Journal of Infectious Diseases*	2021	625 (6)
4	Follow-up of adults with noncritical COVID-19 two months after symptom onset	C. Carvalho-Schneider et.al	*Nature Reviews Rheumatology*	2021	502 (7)
5	The cGAS–STING pathway drives type I IFN immunopathology in COVID-19	J.D. Domizio et.al	*Journal of Autoimmunity*	2022	290 (8)
6	Pembrolizumab versus placebo as adjuvant therapy in completely resected stage IIB or IIC	J.J. Luke et.al	*JAMA Dermatology*	2022	267 (9)

	melanoma (KEYNOTE-716): a randomised, double-blind, phase 3 trial				
7	Investigation of long covid prevalence and its relationship to epstein-barr virus reactivation	Gold, J.E. et.al	*Journal of Infection*	2021	204 (10)
8	Systemic and organ-specific immune-related manifestations of COVID-19	M. Ramos-Casals et.al	*The Lancet Infectious Diseases*	2021	195 (11)
9	Clinical manifestations of COVID-19 in the general population: systematic review	R. da Rosa Mesquita et.al	*Advances in Wound Care*	2021	195 (12)
10	Long-term complications of COVID-19	A.D. Desai et.al	*Journal of the European Academy of Dermatology and Venereology*	2022	186 (13)
11	Long COVID, a comprehensive systematic scoping review	H. Akbarialiabad et.al	*Journal of Clinical Medicine*	2021	183 (14)
12	Skin Manifestations Associated with COVID-19: Current Knowledge and Future Perspectives	G. Genovese et.al	*Food and Chemical Toxicology*	2021	171 (15)
13	Cutaneous reactions after SARS-CoV-2 vaccination: a cross-sectional Spanish nationwide study of 405 cases*	A.Català et.al	*JAAD International*	2022	168 (16)
14	Cutaneous findings following COVID-19 vaccination: review of world literature and own experience	T. Gambichler et.al	*Journal of the European Academy of Dermatology and Venereology*	2022	149 (17)
15	Clinical update on COVID-19 for the emergency clinician: Presentation and evaluation	B. Long et.al	*Oral Diseases*	2022	148 (18)
16	COVID-19 vasculitis and novel vasculitis mimics	D. McGonagle et.al	*Journal of Clinical Medicine*	2021	124 (19)
17	Dermatomyositis With Anti-MDA5 Antibodies: Bioclinical Features, Pathogenesis and Emerging Therapies	A.Nombel et.al	*American Journal of Physiology - Cell Physiology*	2021	118 (20)

18	Incidence and risk factors for persistent symptoms in adults previously hospitalized for COVID-19	D.Munblit et.al	*Frontiers in Immunology*	2021	117 (21)
19	The conundrum of 'long-covid-19': A narrative review	M.Garg et.al	*Journal of the European Academy of Dermatology and Venereology*	2021	116 (22)
20	Clinical and pathologic correlation of cutaneous COVID-19 vaccine reactions including V-REPP: A registry-based study	DE. McMahon et.al	*Nature*	2022	110 (23)
21	Clinical manifestation and disease progression in COVID-19 infection	Tsai, P.-H. et.al	*Journal of the American Academy of Dermatology*	2021	106 (24)
22	Multi-organ involvement in covid-19: Beyond pulmonary manifestations	V. Thakur et.al	*American Journal of Emergency Medicine*	2021	102 (25)
23	COVID-19 Vaccines and the Skin: The Landscape of Cutaneous Vaccine Reactions Worldwide	Q. Sun et.al	*British Journal of Dermatology*	2021	95 (26)
24	Skin manifestations of COVID-19: A worldwide review	Tan, S.W. et.al	*JAMA Network Open*	2021	92 (27)
25	Long COVID in the skin: a registry analysis of COVID-19 dermatological duration	McMahon, D.E. et.al	*Journal of the European Academy of Dermatology and Venereology*	2021	90 (28)
26	Cutaneous manifestations of COVID-19: A systematic review	Singh, H. et.al	*Dermatologic Clinics*	2021	86 (29)
27	Clinical, Laboratory, and Interferon-Alpha Response Characteristics of Patients with Chilblain-like Lesions during the COVID-19 Pandemic	Hubiche, T. et.al	*Journal of the American Academy of Dermatology*	2021	85 (30)
28	The differing patho-physiologies that underlie COVID-19-associated perniosis and thrombotic retiform purpura: a case series	C.M. Magro et.al	*International Journal of General Medicine*	2021	83 (31)
29	Autoimmune and Rheumatic Manifestations Associated with	Tang, K.-T. et.al	*Journal of the American Academy of Dermatology*	2021	73 (32)

	COVID-19 in Adults: An Updated Systematic Review				
30	The JANUS of chronic inflammatory and auto-immune diseases onset during COVID-19 – A systematic review of the literature	Novelli, L. et.al	*Annual Review of Medicine*	2021	73 (33)
31	Skin manifestations of the BNT162b2 mRNA COVID-19 vaccine in healthcare workers. 'COVID-arm': a clinical and histological characterization	Fernandez-Nieto, D. et.al	*Pathogens*	2021	70 (34)
32	Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs	Seneff, S. et.al	*Rheumatology International*	2022	69 (35)
33	Cutaneous adverse reactions associated with sars-cov-2 vaccines	Bellinato, F. et.al	*Journal of the Chinese Medical Association*	2021	67 (36)
34	Can the SARS-CoV-2 infection trigger systemic lupus erythematosus? A case-based review	Gracia-Ramos, A.E. et.al	*Nature Medicine*	2021	66 (37)
35	Silent COVID-19: what your skin can reveal	Guarneri, C. et.al	*Clinical Microbiology and Infection*	2021	66 (38)
36	Psoriasis flare-up associated with second dose of Pfizer-BioNTech BNT16B2b2 COVID-19 mRNA vaccine	Krajewski, P.K. et.al	*Nature Communications*	2021	65 (39)
37	Incidence of Cutaneous Reactions after Messenger RNA COVID-19 Vaccines	Robinson, L.B. et.al	*The Lancet*	2021	65 (40)
38	Causation or confounding: why controls are critical for characterizing long COVID	Amin-Chowdhury, Z. et. al	*Clinical and Experimental Dermatology*	2021	65 (41)
39	Variant-specific symptoms of COVID-19 in a study of 1,542,510 adults in England	Whitaker, M. et.al	*JAMA Dermatology*	2022	62 (42)
40	Sulodexide in the Treatment of Patients with Early Stages of COVID-19: A Randomized Controlled Trial	Gonzalez-Ochoa, A.J. et.al	*Nature*	2021	62 (43)

41	Post-COVID-19 Condition	Nalbandian, A. et.al	*Frontiers in Immunology*	2023	61 (44)
42	SARS-CoV-2-induced telogen effluvium: a multicentric study	Moreno-Arrones, O.M. et. al	*The Lancet Rheumatology*	2021	60 (45)
43	Mucocutaneous Manifestations of Multi-system Inflammatory Syndrome in Children during the COVID-19 Pandemic	Young, T.K. et.al	*Nature Medicine*	2021	59 (46)
44	Transient cutaneous manifestations after administration of Pfizer-BioNTech COVID-19 Vaccine: an Italian single-centre case series	M.Corbeddu. et.al	*British Journal of Dermatology*	2021	58 (47)
45	Clinical, virological and imaging profile in patients with prolonged forms of COVID-19: A cross-sectional study	D. Salmon-Ceron et. al	*Dermatology*	2021	58 (48)
46	Efficacy and Safety of Cannabidiol plus Standard Care vs Standard Care Alone for the Treatment of Emotional Exhaustion and Burnout among Frontline Health Care Workers during the COVID-19 Pandemic: A Randomized Clinical Trial	JAS Crippa et.al	*JAMA Dermatology*	2021	57 (49)
47	The clinical spectrum of COVID-19–associated cutaneous manifestations: An Italian multicenter study of 200 adult patients	A.V. Marzano et.al	*Thrombosis and Haemostasis*	2021	57 (50)
48	Skin manifestations of COVID-19 in children: Part 1	D. Andina et.al	*Infection*	2021	57 (51)
49	Oral cavity lesions as a manifestation of the novel virus (COVID-19)	R. Ansari et.al	*Clinical and Experimental Allergy*	2021	57 (52)
50	Positive impact of oral hydroxychloroquine and povidone-iodine throat spray for COVID-19 prophylaxis: An open-label randomized trial	Seet, R.C.S. et.al	*International Journal of Infectious Diseases*	2021	55 (53)

were cohort studies, 3 (6%) were cross-sectional studies, 4 (8%) were descriptive studies, with the majority being 12 (24%) consisting of systematic reviews, and the remaining 8 (16%) of various other types. The data are presented in the table below and subsequently illustrated in the following chart.

Countries with the highest number of publications among the most cited articles are the USA (13), followed by Spain and Italy (respectively 7 papers), France 4, India and Japan 3 papers respectively, UK 3 articles, Germany, Brazil, China, Iran 2 articles respectively, Mexico, Russia and Poland from 1 paper.

The epidemiology is mentioned in 30%, while the remaining 35 articles (70%) do not reference epidemiology in their discussions. In this study was observed that a large portion of the articles focused on the description of various signs and symptoms. Specifically, 86% of papers, primarily focused on the clinical characteristics and diagnosis, while the remaining 14% had clinical characteristics as a secondary focus. The clinical characteristics, together with the diagnosis, remained a key aspect of the validity of the link between cutaneous manifestations and COVID-19 infection. Clinical characteristics and diagnosis are mentioned in 86% of the 50 most cited articles, while the remaining 14% do not refer to them. Only 36%, had a primary focus on the pathophysiology and the detailed description of the link between cutaneous manifestations and COVID-19, while 64%, had pathophysiology as a secondary topic. It was found that only 28% of articles referred to comorbidities along with clinical characteristics and diagnosis as part of their analysis to confirm the link between cutaneous manifestations and COVID-19, meanwhile, 72% had comorbidities as a secondary focus. Treatment was the focus on 34%, while 66% have treatment as a secondary focus. Pathogenesis is discussed in 36%, while the remaining 64% do not consider pathogenesis as a primary issue. Comorbidities are referenced in only 28% of the articles.

Skin manifestations related to SARS-CoV-2 infection can be divided mainly into five groups: chilblain-like lesions (CBLLs), maculopapular eruptions, urticarial eruptions, vesicular eruptions, and livedo or necrosis. The results were derived from a series of 207 cases that were reviewed, most of which were described as case reports or systematic studies.

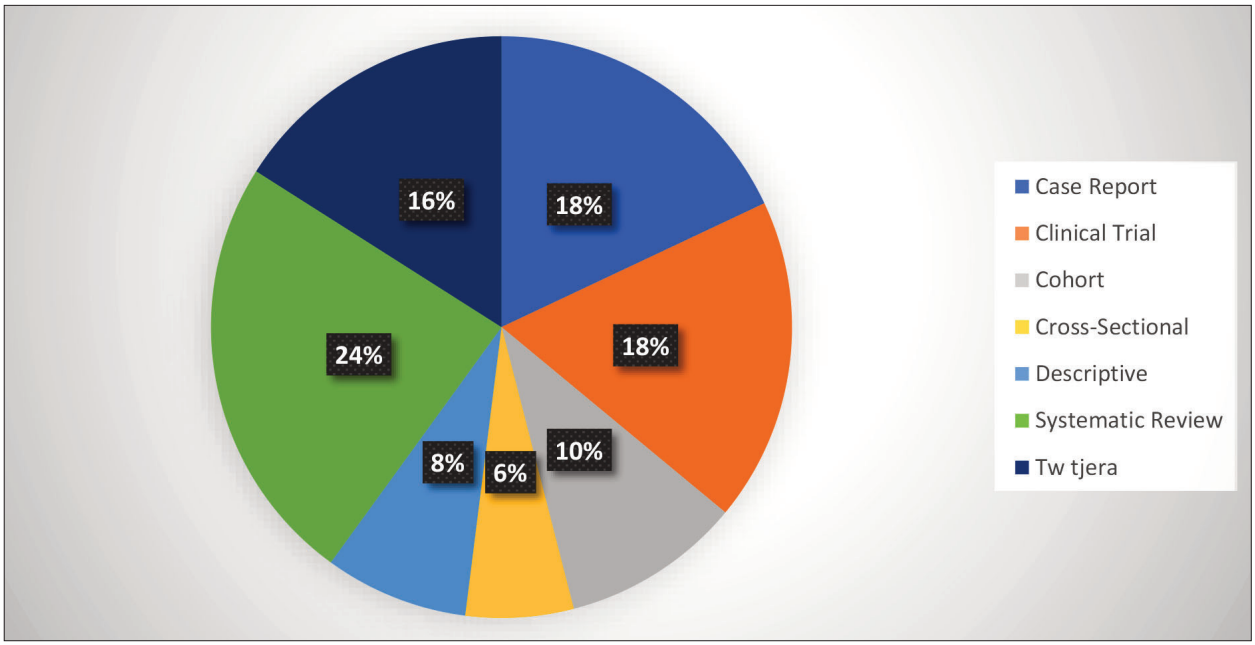

Figure 2. Percentage of articles based on their study design.

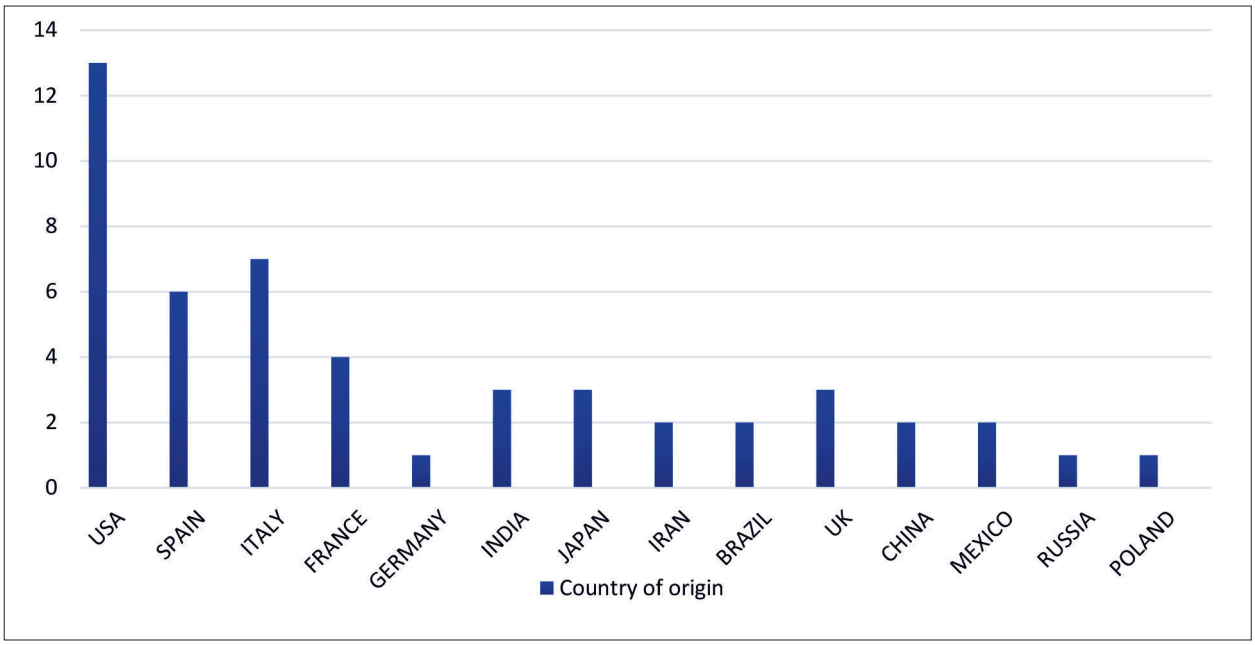

Figure 3. Number of articles based on country of origin

These clinical findings can further be classified as inflammatory lesions (maculopapular/morbilliform, urticarial, and vesicular) or vascular lesions (pernio-like, petechial/purpuric, and livedoid).

From a total of 207 cases included in the study, it was concluded that 115 cases (55.5%) were male, and 92 cases (44.5%) were female. A predominance of male patients over female patients was observed, with a male-to-female ratio of 1.25. The average age of male patients was 27 years old, with an age range of 2–98 years. The average age of the female patients was 32 years old, with an age range of 4–86 years. As part of this analysis, it seems that there is a strong connection between skin manifestations and Covid-19 infection.

Table 2. Skin manifestations and Covid-19 among 277 cases in 50 most cited articles

TYPES OF SKIN MANIFESTATIONS	NR. OF CASES AND PERCENTAGE
MACULOPAPULAR/MORBILLIFORM LESIONS	19 cases (9%)
URTICARIAL LESIONS	20 cases (9.6%)
CHILBLAIN-LIKE LESIONS (COVID TOES)	76 cases (36.7%)
VESICULAR LESIONS	33 cases (15.9%)
PETECHIAL/PURPURIC LESIONS	5 cases (2.4%)
LIVEDOID LESIONS	3 cases (1.5%)
ACRAL LESIONS	17 cases (8.2%)
OTHER	34 cases (16.4%)

Discussions

This bibliometric analysis of the 50 most cited articles on cutaneous manifestations in COVID-19 patients highlights the complexity and significance of dermatological manifestations in the context of a global pandemic. Skin manifestations have emerged as an early signal of infection and, in some cases, as an important indicator of systemic involvement or more serious complications, reflecting a notable increase in interest and citations in the scientific literature.

The findings from this analysis show that a significant portion of early research focused on documenting and describing dermatological manifestations of COVID-19. These manifestations range from common maculopapular rashes and urticaria to more unusual lesions such as chilblain-like lesions and livedo reticularis, which have garnered particular interest due to their possible connection with vascular pathologies and microvascular thrombosis. These manifestations not only aid in identifying infected patients but also provide valuable insight into the pathophysiological mechanisms of the disease, suggesting that SARS-CoV-2 may cause extensive vascular damage and systemic inflammation . For instance, several important studies have suggested that skin manifestations, such as chilblain-like lesions ("COVID toes"), may result from vascular dysfunction and microvascular thrombosis, which are key characteristics of SARS-CoV-2 infection. Moreover, it is important to emphasize that the most cited studies are not limited to clinical descriptions but also include systematic reviews and meta-analyses that have consolidated the acquired knowledge and provided a robust framework for further research. These studies have been crucial in developing clinical guidelines that assist physicians in accurately identifying and managing dermatological manifestations of COVID-19.

Another critical aspect of the discussion is that skin manifestations may serve as indicators for the prognosis of COVID-19 patients. The estimated incidence of cutaneous manifestations secondary to COVID-19 is between 4% and 20.4%. Some studies included in this analysis have revealed that patients with certain skin manifestations, particularly those associated with vasculopathy, may have an increased risk of more severe complications, such as cardiovascular diseases and respiratory failure. This suggests that dermatological manifestations may play an important role in risk stratification and guiding therapeutic decisions.

The analysis also reveals a strong trend towards international collaborative publications, particularly from Europe and North America, reflecting the global nature of the pandemic and the need for extensive scientific collaboration. This has led to rapid knowledge exchange and improved clinical practices regarding the diagnosis and management of skin manifestations. Furthermore, the involvement of experts from diverse fields such as dermatology, infectious diseases, and immunology has contributed to a more comprehensive understanding of the impact of COVID-19 on the skin and beyond.

Ultimately, the role of dermatological manifestations in COVID-19 is multifaceted. They not only provide valuable diagnostic and prognostic information but also contribute to a comprehensive understanding of the disease pathology and the improvement of patient care. As the pandemic continues to evolve, it is clear that skin manifestations will remain a critical area of research and clinical attention, requiring ongoing focus and further exploration.

Conclusions

This bibliometric analysis provides a detailed overview of the development and impact of the scientific literature on skin manifestations related to COVID-19. The results indicate that dermatological manifestations of SARS-CoV-2 are a growing and highly significant field, which has greatly contributed to our comprehensive understanding of this complex disease. One of the most important conclusions is that dermatological manifestations may serve as early indicators or warning signs of systemic involvement of the infection, suggesting that skin examination should be a crucial component in the overall assessment of COVID-19 patients. In the future, it is essential for research to continue focusing on exploring the pathophysiological mechanisms of these skin manifestations and their connections with the immune and vascular systems. Furthermore, given that the pandemic is still evolving, it is important to monitor and study the long-term dermatological effects of COVID-19 to ensure appropriate patient management in the future.

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Conflict of interest
NONE DECLARED

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