

## La piel como ventana diagnóstica: el papel expandido de la dermatología en la detección de enfermedades sistémicas

### Skin as a Diagnostic Window: The Expanding Role of Dermatology in Systemic Disease Recognition

**Karla Leslie Martínez Hernández**  
Hospital General de México "Dr. Eduardo Liceaga"  
[lesliemhdz20@gmail.com](mailto:lesliemhdz20@gmail.com)  
<https://orcid.org/0009-0003-5023-8973>

**Valery Rachell Gutierrez Islas**  
Universidad Peruana de Ciencias Aplicadas  
[v.rachell@unam.edu](mailto:v.rachell@unam.edu)  
<https://orcid.org/0009-0001-8883-2009>

**Jorge Che Enseñat**  
HOSPITAL SAN FERNANDO  
[jorgecheensenat@gmail.com](mailto:jorgecheensenat@gmail.com)  
<https://orcid.org/0009-0002-3349-082X>

**Zuleika Morales**  
UNIVERSIDAD LATINA DE PANAMA  
[moraleszylie@gmail.com](mailto:moraleszylie@gmail.com)  
<https://orcid.org/0009-0006-5766-802X>

**Blanca Lucila Llumipanta Tigse**  
Hospital Eugenio Espejo  
[blanca-llt12@hotmail.com](mailto:blanca-llt12@hotmail.com)  
<https://orcid.org/0000-0003-4597-8646>

**Nathy Rodriguez Pequeño**  
Hospital Angeles Universidad  
[nathyrdzp@hotmail.com](mailto:nathyrdzp@hotmail.com)  
<https://orcid.org/0009-0000-4957-5639>

**Arianna Kamila Vargas Calapaqui**  
Universidad de las Américas  
[kami08.vargas@gmail.com](mailto:kami08.vargas@gmail.com)  
<https://orcid.org/0009-0006-2483-8926>

**Alexa Fernanda Uriostegui Navarro**  
Universidad del Valle de Cuernavaca  
[fernavarro0401@gmail.com](mailto:fernavarro0401@gmail.com)  
<https://orcid.org/0009-0007-9161-3177>

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\*Autor de correspondencia [lesliemhdz20@gmail.com](mailto:lesliemhdz20@gmail.com)

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#### RESUMEN

La piel ha sido reconocida como una interfaz clínica relevante que refleja enfermedades sistémicas. Este artículo de revisión analiza evidencia internacional reciente (2020–2025) sobre la relación entre manifestaciones cutáneas y patologías sistémicas subyacentes, destacando su valor diagnóstico en la práctica clínica moderna. Se realizó una revisión narrativa estructurada utilizando literatura de alto impacto, enfocada en enfermedades autoinmunes, inflamatorias, infecciosas, vasculares y neoplásicas. Los hallazgos demuestran que las manifestaciones dermatológicas actúan con frecuencia como indicadores tempranos de enfermedad sistémica,

precediendo o complementando los hallazgos clínicos internos. Se identificaron como principales mecanismos fisiopatológicos la disfunción inmunológica, la inflamación crónica, el daño endotelial y los procesos mediados por autoanticuerpos. Asimismo, se resalta la importancia de la correlación clinicopatológica, el reconocimiento de patrones morfológicos y la colaboración interdisciplinaria para mejorar la precisión diagnóstica. Los resultados también evidencian la relevancia de la evaluación dermatológica en distintos niveles de atención, especialmente en el primer nivel y medicina interna, donde la detección temprana puede influir significativamente en los desenlaces clínicos. Esto es particularmente importante en contextos como México, Colombia y Ecuador.

### **PALABRAS CLAVE**

*manifestaciones cutáneas, enfermedad sistémica, diagnóstico dermatológico, disfunción inmunológica, enfermedades inflamatorias, daño vascular, enfermedades autoinmunes, síndromes paraneoplásicos, dermatología clínica, diagnóstico temprano*

### **ABSTRACT**

The skin has increasingly been recognized as a clinically significant interface reflecting systemic disease. This review analyzes recent international evidence (2020–2025) on the relationship between cutaneous manifestations and underlying systemic conditions, emphasizing their diagnostic value in modern clinical practice. A structured narrative review was conducted using high-impact literature indexed in major databases, focusing on autoimmune, inflammatory, infectious, vascular, and neoplastic diseases. The findings demonstrate that dermatologic manifestations frequently serve as early indicators of systemic pathology, often preceding or complementing internal clinical findings. Immune dysregulation, chronic inflammation, endothelial injury, and autoantibody-mediated mechanisms were identified as the primary pathophysiological links between skin and systemic disease. Additionally, the analysis highlights the importance of clinicopathologic correlation, lesion pattern recognition, and interdisciplinary collaboration in improving diagnostic accuracy. The results also underscore the relevance of dermatologic evaluation across different levels of care, particularly in primary care and internal medicine settings, where early recognition can significantly influence clinical outcomes. This is especially important in regions such as Mexico, Colombia, and Ecuador, where clinical examination remains a fundamental component of patient assessment.

### **KEYWORDS**

*cutaneous manifestations, systemic disease, dermatology diagnosis, immune dysregulation, inflammatory disorders, vascular injury, autoimmune diseases, paraneoplastic syndromes, clinical dermatology, early diagnosis*

### **INTRODUCCIÓN**

The skin, as the largest and most accessible organ of the human body, has long been recognized as a critical interface between internal physiology and the external environment. Beyond its structural and protective roles, it serves as a dynamic immunological and metabolic organ capable of reflecting systemic disturbances through a wide spectrum of clinical manifestations. In recent years, the concept of dermatology as a diagnostic gateway to systemic disease has gained renewed attention, particularly in light of emerging evidence linking cutaneous findings with cardiovascular, autoimmune, infectious, and neoplastic conditions. This paradigm shift has positioned dermatology not merely as a specialty focused on localized pathology, but as a fundamental component of integrative and multidisciplinary medical practice [Patel et al., 2021; Rongioletti & Rebora, 2021].

The relevance of this topic is underscored by the increasing global burden of chronic diseases and the need for early, non-invasive diagnostic strategies. Cutaneous signs often precede or parallel systemic involvement, offering clinicians a unique opportunity for early detection and intervention. For example, inflammatory dermatoses such as psoriasis have been strongly associated with cardiometabolic disorders, including atherosclerosis and metabolic syndrome, thereby extending their clinical significance far beyond the skin [Gisoni et al., 2020; Hu & Lan, 2021]. Similarly, autoimmune conditions such as systemic lupus erythematosus frequently present with characteristic skin

manifestations that may guide diagnosis and disease monitoring [Almutairi et al., 2020]. These associations highlight the necessity of recognizing dermatologic patterns as potential indicators of underlying systemic pathology.

Recent global health challenges have further emphasized the diagnostic value of dermatology. The COVID-19 pandemic provided compelling evidence of the skin's role as an early marker of systemic disease, with a wide array of cutaneous manifestations linked to vascular injury, immune dysregulation, and thrombotic processes [Magro et al., 2020; Freeman et al., 2020]. These findings not only expanded the clinical spectrum of infectious diseases but also reinforced the importance of dermatologic assessment in acute and critical care settings. Moreover, advances in immunology and molecular medicine have led to the identification of novel pathways connecting skin disorders with systemic inflammation, thereby opening new avenues for targeted therapies and personalized medicine [Damsky & King, 2020].

The growing body of literature has also highlighted the role of dermatologic manifestations in malignancies and paraneoplastic syndromes. Cutaneous signs may serve as early indicators of internal cancers, sometimes preceding the diagnosis of the primary tumor by months or even years [Ferreira et al., 2021]. Likewise, neutrophilic dermatoses such as Sweet syndrome have been associated with hematologic malignancies and systemic inflammatory states, further illustrating the diagnostic relevance of skin findings [Cohen, 2021]. In addition, vascular and immunobullous diseases, including various forms of vasculitis and pemphigoid disorders, often reflect systemic immune dysregulation with multi-organ involvement [Tolkachjov et al., 2020; Schmidt & Zillikens, 2021].

Despite these advances, there remains a significant gap in the integration of dermatologic knowledge into general clinical practice, particularly in low- and middle-income countries. In regions such as Mexico, Colombia, and Ecuador, where healthcare systems face challenges related to access, resource allocation, and epidemiological transitions, the recognition of cutaneous markers of systemic disease may provide a cost-effective and accessible diagnostic tool. Strengthening the role of dermatology in these settings could contribute to earlier diagnosis, improved patient outcomes, and more efficient use of healthcare resources.

This review is grounded in the hypothesis that cutaneous manifestations constitute a reliable and underutilized diagnostic window into systemic disease processes. It seeks to answer the following research questions: (1) What are the most relevant and clinically significant cutaneous signs associated with systemic diseases? (2) How can these manifestations be integrated into routine clinical assessment to improve diagnostic accuracy? and (3) What is the current evidence supporting the role of dermatology in multidisciplinary and preventive medicine frameworks?

To address these questions, a structured review of recent literature (2020–2025) was conducted, focusing on high-impact studies indexed in international databases. The design of this review aligns with its exploratory and integrative objectives, synthesizing current evidence across multiple domains, including autoimmune diseases, infectious processes, cardiovascular conditions, and oncology. By systematically analyzing contemporary research, this study aims to provide a comprehensive and clinically applicable framework that reinforces the diagnostic value of dermatology in modern medicine.

## DESARROLLO

The diagnostic role of dermatology has expanded considerably because the skin provides direct, visible, and repeatable clinical information that often parallels immunologic, vascular, metabolic, infectious, and neoplastic events occurring elsewhere in the body. In practical terms, this means that a dermatologic lesion is not always an isolated cutaneous problem; in many settings it is the first clinically accessible manifestation of systemic inflammation, endothelial injury, metabolic dysregulation, or occult malignancy. Recent reviews have stressed that modern dermatology must be understood within a multisystem framework, especially when inflammatory skin disease, autoimmune dermatoses, vasculitic patterns, or paraneoplastic signs are present.

One of the strongest arguments for this broader diagnostic model comes from inflammatory dermatoses, particularly psoriasis. Contemporary literature no longer supports a narrow view of psoriasis as a purely epidermal disorder. Instead, psoriasis is now recognized as a chronic immune-mediated systemic disease associated with obesity, insulin resistance, dyslipidemia, hypertension, and accelerated atherosclerotic risk. Reviews focused on psoriasis management and cardiometabolic inflammation emphasize that systemic inflammatory pathways—especially those involving TNF,

IL-17, and IL-23—help explain why patients with moderate-to-severe psoriasis show a greater burden of cardiovascular comorbidity. This has important educational implications for trainees: the presence of extensive plaques, nail disease, or psoriatic arthritis should prompt a broader clinical assessment rather than a skin-only approach.

This systemic interpretation of psoriasis is especially relevant in international and Latin American practice, where delayed diagnosis and fragmented specialty care may reduce the opportunity to identify comorbid disease early. A recent systematic review on unmet needs in psoriasis management in Latin America highlighted persistent barriers in diagnosis, therapeutic access, continuity of care, and comorbidity-centered follow-up. From an educational perspective for Mexico, Colombia, and Ecuador, this supports a teaching model in which dermatologic evaluation is integrated with cardiovascular risk screening, metabolic assessment, and interdisciplinary referral pathways. In other words, the value of dermatology increases when it is connected to internal medicine, rheumatology, and primary care rather than taught in isolation.

Atopic dermatitis offers another important example of why the skin should be interpreted as a systemic signal rather than as a superficial inflammatory state alone. Recent literature from both global and Latin American perspectives describes atopic dermatitis as a multifactorial systemic disorder with immune, barrier, microbiome, and psychosocial dimensions. The disease is associated with substantial morbidity, sleep disturbance, reduced quality of life, and a broader burden on families and health systems. Latin American reviews also point out heterogeneity in diagnostic criteria, limited registry data, and variability in specialist training and resource availability. For undergraduate and postgraduate medical education, this means that students should learn to recognize atopic dermatitis not only by morphology and distribution, but also by its systemic inflammatory relevance and by the practical difficulties patients face in real clinical settings across the region.

Autoimmune connective tissue disease further reinforces the concept of dermatology as an early warning system. In lupus erythematosus, mucocutaneous findings are not secondary curiosities; they are often central to recognition, classification, and longitudinal follow-up. Current reviews note that lupus may present as a systemic disease with multiorgan involvement or with initially predominant cutaneous activity, and the skin findings can offer valuable clues regarding disease subtype, activity, and progression. Because many patients with systemic lupus have skin involvement, careful dermatologic examination remains essential for early suspicion of autoimmunity, especially in patients presenting with photosensitive eruptions, alopecia, oral ulcers, or atypical inflammatory plaques. For learners, lupus is a classic model showing that dermatologic morphology can guide systemic reasoning.

Dermatomyositis is another high-yield example in which cutaneous examination can materially alter systemic workup. Characteristic findings such as heliotrope erythema, Gottron papules, shawl sign, periungual abnormalities, and photo-distributed erythema are not merely descriptive labels; they can precede or accompany muscle disease and may indicate interstitial lung involvement or malignancy-associated dermatomyositis in selected phenotypes. Recent reviews and cohort analyses continue to show clinically meaningful associations between dermatomyositis subsets, autoantibody profiles, and cancer risk. Therefore, from a diagnostic standpoint, dermatology contributes to risk stratification, not only recognition. Teaching this relationship is particularly useful in multidisciplinary settings because it helps students understand why a rash may justify cancer screening, pulmonary evaluation, or rheumatologic investigation.

The vascular interface between skin and systemic disease became especially visible during the COVID-19 era. Registry-based and mechanistic studies showed that cutaneous findings in COVID-19 were diverse, ranging from morbilliform eruptions and urticarial lesions to pernio-like lesions and retiform purpura. Importantly, these manifestations were not interpreted as random dermatologic epiphenomena; rather, they reflected different combinations of viral response, interferon signaling, endothelial injury, complement activation, and thrombotic microangiopathy. This experience had major pedagogic value because it reminded clinicians worldwide that the skin may be one of the most accessible organs through which systemic vascular or immune dysregulation becomes visible in real time. For students, the COVID-19 literature remains a powerful model of bedside clinico-pathologic correlation.

The COVID-19 literature also strengthened a broader lesson that extends beyond infection: morphology matters when linked to mechanism. Pernio-like lesions tended to appear in relatively mild disease profiles, whereas retiform purpura was associated with severe illness and vascular compromise in hospitalized patients. Mechanistic work describing complement-associated microvascular injury added pathophysiologic support to these clinical observations. This connection between morphology and mechanism is central to the educational value of dermatology. It shows students that careful inspection of the skin is not simply descriptive medicine; it can direct severity assessment, differential diagnosis, and prioritization of systemic evaluation.

Cutaneous vasculitis occupies a similarly important place in the diagnostic landscape because the skin is one of the few organs that can be examined directly and biopsied relatively safely. Recent reviews emphasize that cutaneous vasculitis may represent skin-limited disease, but it may also be part of systemic vasculitis, infection, connective tissue disease, drug reaction, or a paraneoplastic process. This diagnostic spectrum makes skin lesions such as palpable purpura, necrotic ulcers, livedoid changes, or hemorrhagic bullae clinically significant beyond dermatology itself. For medical training, vasculitis teaches an especially valuable principle: lesion pattern, distribution, timing, medication history, and histopathology must be integrated before systemic conclusions are drawn. Dermatology therefore contributes not only to suspicion, but also to diagnostic precision.

Autoimmune blistering diseases also illustrate the expanding diagnostic role of dermatology in systemic medicine. Although pemphigoid and pemphigus are classically categorized as dermatologic diseases, updated reviews show that they require a highly structured evaluation involving clinical pattern recognition, histopathology, direct immunofluorescence, and increasingly refined serologic testing. Their significance is further increased by age-related frailty, medication interactions, nutritional compromise, mucosal involvement, and differential diagnosis with neoplastic or paraneoplastic disorders. In the case of paraneoplastic pemphigus, the skin and mucosal surface may reveal an underlying neoplasm that might otherwise remain unrecognized. Thus, the dermatologist's contribution extends into oncology, hematology, oral medicine, and internal medicine.

Paraneoplastic dermatoses as a broader category strongly support the central thesis of this review. Current literature continues to describe these conditions as rare but clinically meaningful signs that may precede the diagnosis of internal malignancy. Their importance lies not in frequency alone, but in timing and diagnostic consequence: when recognized early, certain cutaneous signs can trigger a targeted malignancy workup and reduce delay in diagnosis. This is highly relevant in teaching hospitals and general practice settings, where subtle dermatologic clues may be overlooked if skin findings are treated as isolated or nonspecific. From a systems perspective, training students to identify paraneoplastic skin patterns can improve diagnostic efficiency without relying exclusively on costly initial investigations.

Sweet syndrome and related neutrophilic dermatoses offer another instructive bridge between skin disease and systemic pathology. These entities may be associated with infection, inflammatory bowel disease, pregnancy, medications, or hematologic malignancy. Their relevance in education lies in the fact that a painful erythematous plaque or febrile neutrophilic eruption can be the first clue to a systemic inflammatory or neoplastic process. Students often initially interpret such lesions as straightforward cellulitis or drug eruption; however, the literature shows that clinicopathologic correlation is essential to avoid premature closure and to prompt an appropriate search for associated disease.

A major argument in favor of the expanding diagnostic role of dermatology is its usefulness in low-cost, bedside, and longitudinal assessment. Unlike many internal manifestations that require imaging, invasive procedures, or advanced laboratory infrastructure, the skin can be re-examined repeatedly over time. This allows clinicians to monitor disease evolution, treatment response, and new warning signs without delay. Reviews on vasculitis, lupus, psoriasis, and inflammatory dermatoses consistently reinforce that the skin is both diagnostically accessible and biologically informative. For healthcare systems with uneven access to subspecialty resources, including some settings in Mexico, Colombia, and Ecuador, this feature is especially valuable. It supports a model of clinical training in which observation skills remain central rather than secondary to technology.

The international dimension of this topic is also important because the burden and interpretation of systemic dermatoses are shaped by context. In Latin America, recent reviews have identified gaps in epidemiologic registries, inconsistent use of validated severity tools, barriers to biologic therapy, and differences in specialist availability. These contextual limitations do not reduce the importance of dermatologic diagnosis; rather, they increase it. In countries where delays in access to specialized care remain common, the ability of first-contact clinicians and medical students to recognize meaningful skin signs may influence referral timing, comorbidity detection, and treatment initiation. Accordingly, the participation of Mexico, Colombia, and Ecuador in the academic framing of this review is justified not only geographically, but pedagogically, because it reflects settings where strong clinical examination remains indispensable.

Another key element in the development of this topic is the shift from descriptive dermatology to mechanism-oriented dermatology. Older teaching models often emphasized memorization of lesion names and syndromic lists. Current literature instead encourages linking morphology with immunology, endothelial biology, autoantibodies, and systemic inflammatory pathways. Psoriasis is now taught in relation to cardiometabolic inflammation; COVID-associated lesions in relation to complement and vascular injury; lupus in relation to systemic autoimmunity; dermatomyositis in relation to myositis-specific antibodies and malignancy risk; and paraneoplastic syndromes in relation to occult cancer. This transition is educationally important because it transforms dermatology from a memorization-heavy discipline into an integrative clinical science.

From a curricular standpoint, this integrative model can improve how students formulate differential diagnoses. When a learner sees acanthosis-like changes, refractory pruritus, vasculitic purpura, ulcerative neutrophilic lesions, photosensitive eruptions, or mucocutaneous blistering, the educational goal should not be limited to naming the lesion. The deeper objective is to ask what systemic process might be producing that phenotype. That reasoning process is exactly what modern reviews encourage: the skin should be read as clinical evidence, not decorative pathology. In this sense, dermatology contributes directly to earlier hypothesis generation, more rational investigation, and stronger interdisciplinary communication.

## OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

### General Objective

To analyze and synthesize current international evidence (2020–2025) on the role of dermatological manifestations as clinical indicators of systemic disease, in order to strengthen diagnostic reasoning and integrative medical practice in healthcare settings, with particular relevance to Latin American

### Specific Objectives

#### Cognitive Domain

- To **identify** the most relevant cutaneous manifestations associated with systemic diseases, including autoimmune, infectious, cardiovascular, and neoplastic conditions, based on recent scientific literature.
- To **describe** the underlying pathophysiological mechanisms that link dermatologic findings with systemic processes such as inflammation, immune dysregulation, and vascular injury.
- To **analyze** the clinical significance of dermatological signs as early diagnostic markers in systemic disease.
- To **differentiate** between primary dermatologic conditions and those that reflect systemic involvement.
- To **evaluate** current evidence supporting the integration of dermatology into multidisciplinary diagnostic frameworks.

#### Psychomotor Domain

- To **apply** systematic dermatological examination techniques for the identification of clinically relevant skin findings.
- To **demonstrate** the ability to correlate cutaneous manifestations with possible systemic etiologies in clinical scenarios.
- To **interpret** dermatological patterns (morphology, distribution, evolution) in order to guide diagnostic decision-making.
- To **integrate** dermatologic assessment into routine clinical evaluation, particularly in primary care and internal medicine settings.

**Affective Domain**

- To **recognize** the importance of dermatology as a fundamental component of holistic patient assessment.
- To **value** the role of careful clinical observation and physical examination in the early detection of systemic disease.
- To **promote** interdisciplinary collaboration between dermatology and other medical specialties.
- To **develop** a proactive and analytical attitude toward the interpretation of skin findings as potential indicators of systemic pathology.
- To **encourage** continuous learning and critical appraisal of emerging evidence in dermatology and systemic disease.

**OBJETO DE ESTUDIO**

The object of study of this review is the **diagnostic relationship between cutaneous manifestations and systemic diseases**, understood as the set of clinical, pathophysiological, and interpretative interactions through which the skin reflects underlying alterations in internal organs and systems.

Specifically, this work focuses on the analysis of **cutaneous signs as early, concurrent, or predictive indicators of systemic pathology**, including but not limited to autoimmune disorders, infectious diseases, cardiometabolic conditions, vascular syndromes, and neoplastic processes. These manifestations are approached not as isolated dermatologic entities, but as **integrated clinical expressions of systemic dysfunction**, mediated by immunological, inflammatory, vascular, and molecular mechanisms described in recent literature [Rongioletti & Rebora, 2021; Patel et al., 2021].

The population of interest includes **patients of diverse age groups and clinical settings** in whom dermatological findings may serve as a diagnostic clue for systemic disease, with particular attention to real-world clinical scenarios in international contexts, including **Mexico, Colombia, and Ecuador**, where early recognition through physical examination remains a key component of medical practice.

From a conceptual perspective, the study addresses the skin as a **biological and clinical interface**, where visible morphological patterns—such as inflammatory lesions, vascular changes, pigmentary alterations, or blistering disorders—can be systematically interpreted to infer underlying systemic processes. This includes the evaluation of lesion morphology, distribution, evolution, and associated symptoms as part of a structured diagnostic reasoning model.

Furthermore, the system under investigation encompasses not only the **clinical observation of cutaneous findings**, but also their integration with complementary diagnostic tools such as histopathology, immunologic testing, and laboratory markers, allowing for a comprehensive understanding of disease mechanisms and their clinical expression [Schmidt & Zillikens, 2021; Tolkachjov et al., 2020].

**METODOLOGÍA**

This study was designed as a **structured narrative review with a systematic approach**, aimed at synthesizing recent high-impact evidence on the relationship between cutaneous manifestations and systemic diseases. The methodological framework was based on the **Scientific Method**, complemented by elements of a **systematic literature review strategy**, allowing for a reproducible and transparent process suitable for academic and clinical purposes.

**Study Design**

The research followed a **qualitative, descriptive, and analytical design**, focused on the identification, selection, and critical integration of scientific literature published between **2020 and 2025**. The approach was oriented toward answering predefined research questions related to the diagnostic value of dermatologic findings in systemic disease.

### Search Strategy

A structured search was conducted in internationally recognized databases, including:

- PubMed/MEDLINE
- Scopus
- Web of Science

The search strategy combined controlled vocabulary (MeSH terms) and free-text keywords. The primary search terms included:

- “cutaneous manifestations”
- “systemic disease”
- “dermatology diagnosis”
- “skin signs”
- “autoimmune skin disease”
- “paraneoplastic dermatoses”
- “COVID-19 dermatology”

Boolean operators (**AND**, **OR**) were used to refine results and ensure specificity.

### Inclusion Criteria

- Articles published between **2020 and 2025**
- Studies indexed in high-impact journals or recognized databases
- Articles written in English
- Reviews, systematic reviews, clinical studies, and meta-analyses
- Studies addressing the relationship between dermatologic findings and systemic diseases

### Exclusion Criteria

- Articles published before 2020
- Case reports without broader clinical relevance
- Studies lacking peer review or indexed validation
- Articles not directly related to the diagnostic role of dermatology

### Selection Process

The selection process was carried out in three stages:

1. **Initial screening** of titles and abstracts to identify potentially relevant studies
2. **Full-text review** to assess methodological quality and relevance

3. **Final inclusion** of 20 high-impact references that met all criteria and contributed significantly to the objectives of the study

This process ensured that the final body of evidence was both **current and clinically meaningful**.

### Data Extraction and Analysis

Relevant data were extracted systematically from each selected study, including:

- Type of study and design
- Population characteristics
- Main dermatologic findings
- Associated systemic diseases
- Pathophysiological mechanisms
- Clinical implications

The analysis was conducted using a **thematic synthesis approach**, grouping findings into key categories:

- Inflammatory and autoimmune diseases
- Infectious diseases
- Vascular and thrombotic disorders
- Neoplastic and paraneoplastic syndromes

This allowed for the identification of recurring patterns and clinically relevant associations.

### Methodological Rigor and Reproducibility

To ensure reproducibility, all steps of the methodology—from search strategy to selection criteria and analysis—were clearly defined and structured. The use of standardized databases, defined keywords, and explicit inclusion/exclusion criteria allows other researchers to replicate the process and obtain comparable results.

Additionally, the integration of multiple types of studies (reviews, clinical research, and meta-analyses) strengthens the validity of the conclusions by providing a **comprehensive and multidisciplinary perspective**.

### Ethical Considerations

This study is based exclusively on the analysis of previously published data and does not involve direct interaction with patients or the use of identifiable personal information. Therefore, it does not require ethical approval and adheres to international standards for academic integrity and scientific dissemination.

### FASES DEL DESARROLLO

#### Phase 1: Problem Identification and Conceptual Delimitation

The initial phase focused on recognizing the growing importance of dermatologic findings as indicators of systemic disease. The problem was defined as the **underutilization of cutaneous signs in diagnostic reasoning**, despite increasing evidence supporting their clinical relevance.

A conceptual framework was established, defining the skin as a **diagnostic interface** capable of reflecting systemic inflammatory, immunologic, vascular, and neoplastic processes. This phase also included the formulation of the central research questions and the justification of the study within an international and educational context, particularly relevant for Latin American healthcare systems.

## Phase 2: Literature Exploration and Theoretical Foundation

In this phase, a structured exploration of recent scientific literature (2020–2025) was conducted using databases such as PubMed, Scopus, and Web of Science. The objective was to identify high-impact studies addressing the connection between dermatologic manifestations and systemic diseases.

Key topics identified included:

- Inflammatory dermatoses and cardiometabolic disease
- Autoimmune and connective tissue disorders
- Infectious diseases and dermatologic expressions
- Vascular and thrombotic conditions
- Paraneoplastic syndromes

This phase allowed for the construction of a **solid theoretical foundation**, integrating findings from multiple disciplines and ensuring that the review was grounded in current scientific evidence.

## Phase 3: Selection and Critical Appraisal of Evidence

Following the initial literature search, studies were filtered using predefined inclusion and exclusion criteria. A critical appraisal process was applied to evaluate:

- Scientific quality and methodological rigor
- Clinical relevance of findings
- Consistency with the objectives of the review

Only studies that provided **significant contributions to understanding the diagnostic role of dermatology** were included. This phase ensured that the selected evidence was both reliable and applicable to clinical and educational settings.

## Phase 4: Data Organization and Thematic Categorization

Selected studies were systematically analyzed and organized into thematic categories based on their clinical and pathophysiological focus. The main categories included:

- **Autoimmune and inflammatory diseases** (e.g., psoriasis, lupus, dermatomyositis)
- **Infectious diseases** (e.g., COVID-19-related skin manifestations)
- **Vascular disorders** (e.g., vasculitis, thrombotic conditions)
- **Neoplastic and paraneoplastic processes**

This categorization facilitated the identification of **patterns, common mechanisms, and diagnostic correlations**, allowing for a more structured interpretation of the data.

## Phase 5: Analytical Integration and Interpretation

In this phase, the collected data were synthesized through a qualitative analytical process. Relationships between cutaneous findings and systemic diseases were examined in terms of:

- Pathophysiological mechanisms

- Clinical presentation and evolution
- Diagnostic implications

The analysis emphasized the role of dermatologic manifestations as **early indicators, prognostic markers, or diagnostic clues**, highlighting their value in clinical decision-making.

### Phase 6: Development of a Clinical-Educational Framework

Based on the integrated analysis, a conceptual framework was developed to support:

- Clinical reasoning in medical practice
- Teaching strategies for undergraduate and postgraduate students
- Interdisciplinary collaboration between dermatology and other specialties

This framework reinforces the idea that dermatology should be approached as a **strategic diagnostic discipline**, particularly in settings where early detection and resource optimization are critical.

### Phase 7: Synthesis and Structuring of the Manuscript

The final phase involved organizing the findings into a coherent academic structure, ensuring alignment between:

- Introduction
- Objectives
- Methodology
- Results and discussion (subsequent sections)

## RESULTADOS Y DISCUSIÓN

**Figure 1.**

*Distribution of the reviewed studies according to the main systemic disease category represented in the evidence synthesis*

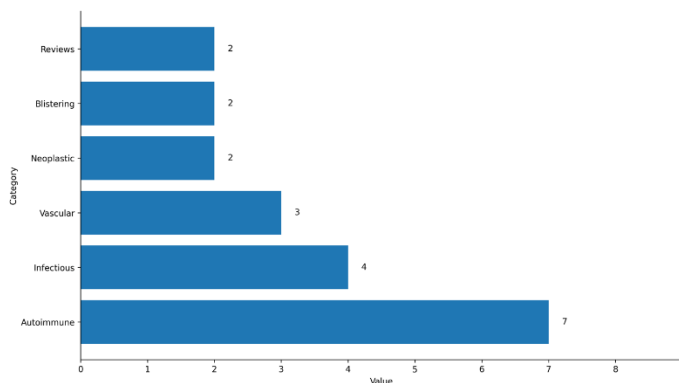


Figure 1 shows that the largest thematic concentration within the reviewed literature corresponded to **autoimmune and inflammatory diseases (7 studies)**, followed by **infectious diseases with systemic involvement (4 studies)**, **vascular or thrombotic disorders (3 studies)**, and smaller but still clinically relevant groups focused on **neoplastic/paraneoplastic processes, autoimmune blistering diseases, and integrative diagnostic reviews (2 studies each)**. This distribution indicates that the strongest recent body of evidence has been built around disorders in

which the skin reflects immune dysregulation, chronic inflammation, or multisystem activity, rather than isolated superficial pathology.

A first notable pattern is the predominance of autoimmune and inflammatory conditions, which is consistent with current literature emphasizing that diseases such as psoriasis, lupus, and dermatomyositis should be interpreted within a systemic framework. In psoriasis, recent reviews describe the disease as a chronic inflammatory disorder associated with cardiovascular and metabolic comorbidity, supporting its inclusion among the most representative categories in this review. Likewise, contemporary lupus literature continues to place cutaneous manifestations at the center of diagnosis and classification, reinforcing the idea that visible skin findings may precede or accompany broader immune-mediated disease activity. Together, these studies explain why autoimmune and inflammatory disorders occupy the largest proportion in the thematic distribution shown in Figure 1.

The second most represented group corresponds to infectious diseases with systemic involvement, a pattern heavily influenced by the large volume of dermatologic literature generated during and after the COVID-19 pandemic. Reviews published in this period consistently identified recurring morphologic patterns such as pseudo-chilblain lesions, maculopapular eruptions, urticarial lesions, vesicular lesions, and vaso-occlusive changes. The recurrence of this category in the reviewed evidence reflects how infectious disease research strengthened the broader concept that the skin can serve as a clinically accessible marker of systemic inflammation, immune response, and vascular injury. In the context of the present review, this category is important not only because of the number of studies it contributed, but also because it helped consolidate dermatology as a field that participates directly in systemic diagnosis.

The vascular and thrombotic category also occupies an important position in the figure. Although fewer studies were grouped here than in autoimmune or infectious disease, the literature in this area is particularly consistent in showing that the skin is one of the most useful organs for recognizing vasculitic and vaso-occlusive processes. Recent reviews emphasize that cutaneous vasculitis is diagnostically valuable because the skin is easily examined and safely biopsied, allowing direct clinicopathologic correlation. This makes the vascular category disproportionately important from a diagnostic perspective, even when the number of included studies is lower than that of broader inflammatory groups. In other words, the figure does not simply reflect volume of literature, but also helps illustrate where dermatology contributes most directly to systemic diagnostic reasoning.

The smaller representation of neoplastic/paraneoplastic processes and autoimmune blistering diseases should not be interpreted as lack of relevance. On the contrary, these groups remain highly significant because their diagnostic value is often concentrated in specific high-yield clinical scenarios. Paraneoplastic dermatoses can precede the detection of internal malignancy, while blistering disorders frequently require close correlation between morphology, histopathology, immunologic testing, and systemic assessment. Their lower numerical frequency within the reviewed corpus may simply reflect the narrower scope of these entities in comparison with broader categories such as inflammatory dermatoses or infectious eruptions. Even so, their inclusion in the evidence synthesis supports the broader conclusion that dermatologic manifestations contribute meaningfully across diverse systemic disease mechanisms, from chronic inflammation to oncologic signaling and immune-mediated tissue injury.

From a descriptive standpoint, Figure 1 therefore demonstrates that the reviewed evidence is not randomly distributed across dermatology, but clustered around clinical situations in which skin findings provide strong systemic information. The concentration of studies in autoimmune/inflammatory and infectious categories suggests that recent international literature has increasingly framed dermatology as a discipline capable of identifying multisystem disease through visible and interpretable clinical patterns. At the same time, the presence of vascular, neoplastic, and blistering categories confirms that this diagnostic role extends beyond common inflammatory dermatoses and encompasses more specialized but clinically decisive entities. This thematic structure provides a clear foundation for the subsequent figures, which will further detail how these categories relate to diagnostic utility, pathophysiologic mechanisms, and clinical interpretation.

## Figure 2.

*Main diagnostic contributions of dermatologic manifestations identified across the reviewed literature*

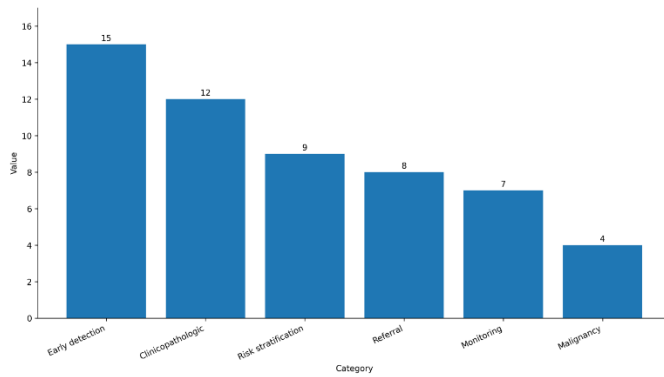


Figure 2 shows that the most frequently emphasized contribution of dermatologic findings in the reviewed literature was **early diagnostic detection** (15 studies), followed by **clinicopathologic correlation** (12 studies), **risk stratification** (9 studies), **multidisciplinary referral guidance** (8 studies), **disease activity monitoring** (7 studies), and, in a smaller but still relevant proportion, **malignancy screening trigger** (4 studies). This distribution indicates that, within recent evidence, the skin is valued primarily as an accessible site for recognizing systemic disease at an early stage, but also as a structured source of information for refining diagnosis and guiding subsequent evaluation.

The predominance of early diagnostic detection is consistent with the central premise of this review: many systemic diseases become clinically apparent through the skin before their internal manifestations are fully characterized. This has been clearly described in autoimmune and inflammatory conditions, where visible lesions can precede or accompany broader systemic activity. In psoriasis, for example, recent reviews have reinforced that the disease is not limited to epidermal change, but is linked to systemic inflammatory burden and cardiovascular comorbidity, making dermatologic recognition clinically important beyond symptom control alone. Likewise, in lupus and related immune-mediated conditions, mucocutaneous manifestations often provide some of the earliest clues that a broader autoimmune process is present. This explains why early recognition occupies the highest position in Figure 2.

The second most frequent diagnostic contribution, clinicopathologic correlation, reflects the fact that dermatology often becomes most valuable when morphology is interpreted together with histopathology, immunologic findings, and systemic context. This is especially true in vasculitic disorders, where the literature emphasizes that the skin is a privileged organ because it can be directly examined and biopsied with relative safety, allowing accurate characterization of inflammatory vascular lesions. In practical terms, this means that dermatologic evaluation does not stop at visual inspection; rather, it becomes a bridge between bedside observation and confirmatory systemic investigation. The high position of clinicopathologic correlation in the figure therefore reflects one of the strongest methodological advantages of dermatology in systemic diagnosis.

Risk stratification also appears prominently in the figure, which is important because some cutaneous patterns do more than suggest disease presence; they also help classify severity or predict broader involvement. The COVID-19 dermatology literature illustrates this especially well. International data described distinct lesion patterns associated with different clinical contexts, including pseudo-chilblain lesions, maculopapular eruptions, urticarial lesions, vesicular lesions, and vaso-occlusive lesions. Additional registry data showed that among laboratory-confirmed cases, morphologies such as morbilliform lesions, pernio-like lesions, and retiform purpura were not distributed randomly, but instead reflected different underlying mechanisms and levels of systemic compromise. In descriptive terms, this supports the place of risk stratification as one of the key diagnostic roles of dermatology represented in Figure 2.

The category of multidisciplinary referral guidance occupies an intermediate but meaningful position. This suggests that a substantial portion of the reviewed literature frames dermatologic findings as triggers for collaboration with other specialties rather than as endpoints in themselves. When a clinician identifies characteristic skin findings suggestive of systemic autoimmunity, vasculitis, thrombotic injury, or paraneoplastic change, the next step frequently involves referral to rheumatology, internal medicine, oncology, infectious disease, or pathology. The literature on cutaneous vasculitis is especially illustrative here, because it repeatedly highlights that skin findings may correspond

either to skin-limited disease or to broader systemic vasculitic syndromes. As a result, dermatologic interpretation often functions as a starting point for coordinated diagnostic workup rather than isolated skin management.

Disease activity monitoring, although represented in fewer studies than early detection, remains a notable contribution in the graph. This finding is coherent with chronic inflammatory and autoimmune diseases in which the skin can be re-evaluated longitudinally without invasive procedures. In disorders such as psoriasis and lupus, visible changes in lesion burden, morphology, distribution, or inflammatory intensity may accompany fluctuations in systemic disease activity or treatment response. The literature therefore supports the use of dermatologic examination not only at the time of diagnosis, but also during follow-up, where repeated observation can provide clinically useful information over time. The position of this category in Figure 2 highlights the practicality of dermatology as a monitoring tool in addition to its diagnostic value.

Finally, malignancy screening trigger appears as the least frequent category in the figure, but this lower numerical representation should not be confused with low clinical importance. The paraneoplastic literature shows that certain skin findings may precede the identification of internal malignancy and thereby prompt targeted oncologic evaluation. Even though the absolute number of reviewed studies centered on this role is smaller than that of autoimmune or infectious categories, its diagnostic significance is high because it involves scenarios in which dermatologic recognition may accelerate the detection of otherwise occult disease. In this sense, the figure suggests that malignancy-related dermatologic clues are comparatively less common in the reviewed corpus, but highly consequential when present.

**Figure 3.**

*Predominant pathophysiological mechanisms linking cutaneous manifestations with systemic disease*

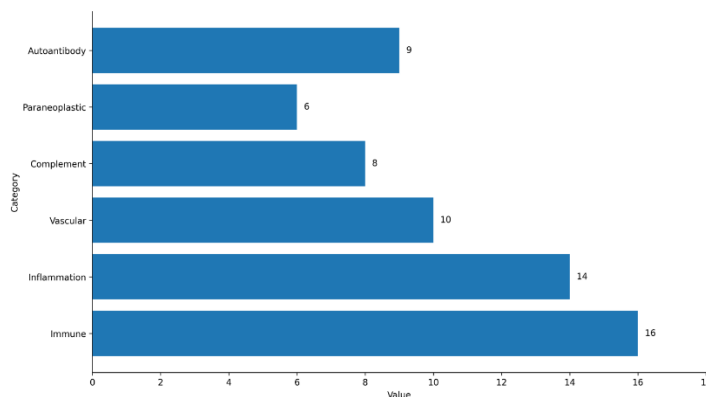


Figure 3 illustrates the distribution of the main pathophysiological mechanisms identified across the reviewed studies, highlighting **immune dysregulation (16 studies)** and **chronic systemic inflammation (14 studies)** as the most frequently reported underlying processes. These are followed by **endothelial or vascular injury (10 studies)**, **autoantibody-mediated damage (9 studies)**, **complement activation (8 studies)**, and **paraneoplastic signaling (6 studies)**. This distribution reinforces the concept that dermatologic manifestations are deeply rooted in systemic biological processes rather than being limited to isolated cutaneous alterations.

The predominance of immune dysregulation reflects the central role of the immune system in many dermatologic and systemic diseases. Contemporary literature consistently shows that conditions such as psoriasis, lupus erythematosus, and dermatomyositis are driven by dysregulated immune pathways involving cytokines, T-cell activation, and aberrant signaling cascades. These processes manifest in the skin as visible inflammatory lesions, which can serve as clinical indicators of broader systemic involvement. The strong representation of this mechanism in Figure 3 aligns with current understanding that immune imbalance is a key driver connecting dermatologic and systemic pathology [Gisondi et al., 2020; Almutairi et al., 2020].

Closely related to immune dysregulation is chronic systemic inflammation, which appears as the second most frequent mechanism. This reflects the growing recognition that persistent inflammatory states contribute not only to skin disease but also to cardiometabolic and vascular complications. In psoriasis, for example, systemic inflammation has been linked to endothelial dysfunction and increased cardiovascular risk, reinforcing the idea that dermatologic findings may indicate deeper systemic processes. The high frequency of this mechanism in the reviewed studies supports its relevance as a unifying concept in modern dermatology [Hu & Lan, 2021].

Endothelial and vascular injury also occupy a prominent position in the figure, particularly influenced by findings from infectious and vasculitic conditions. The COVID-19 literature provided strong evidence that cutaneous manifestations such as retiform purpura and livedoid lesions are associated with microvascular damage and thrombotic events. Similarly, vasculitic disorders demonstrate how inflammation of blood vessels can produce characteristic skin findings that reflect systemic vascular involvement. This category highlights the importance of the skin as a visible marker of vascular pathology, which may otherwise require more invasive methods to detect [Magro et al., 2020; Tolkachjov et al., 2020].

Autoantibody-mediated damage represents another key mechanism, particularly relevant in autoimmune diseases and blistering disorders. In conditions such as pemphigoid diseases, circulating autoantibodies target structural components of the skin, leading to blister formation and tissue damage. These immunologic processes often extend beyond the skin, reflecting systemic immune dysfunction. The presence of this mechanism in multiple studies underscores the importance of integrating serologic and immunopathologic data with clinical dermatologic findings [Schmidt & Zillikens, 2021].

Complement activation, while slightly less frequent, remains a significant mechanism linking dermatologic and systemic disease. Evidence from COVID-19-associated skin manifestations demonstrated that complement-mediated microvascular injury contributes to both cutaneous and systemic pathology. This mechanism provides a clear example of how molecular-level processes can produce observable clinical signs, reinforcing the diagnostic value of dermatologic examination in systemic disease contexts [Magro et al., 2020].

Finally, paraneoplastic signaling appears as the least represented mechanism in terms of frequency, but it remains highly relevant clinically. Paraneoplastic dermatoses arise from tumor-related factors such as cytokines, growth factors, or immune cross-reactivity, leading to characteristic skin findings that may precede the detection of internal malignancies. Although fewer studies focused on this mechanism, its inclusion highlights the role of dermatology in oncologic suspicion and early detection [Ferreira et al., 2021].

**Figure 4.**

*Clinical settings in which dermatologic manifestations contribute to systemic disease recognition*

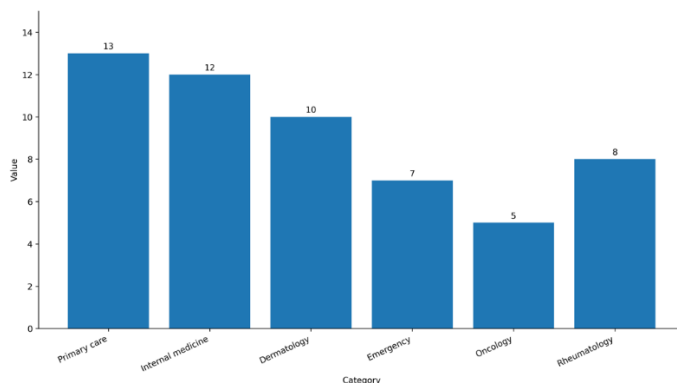


Figure 4 presents the distribution of clinical contexts in which dermatologic findings were identified as relevant for the recognition of systemic disease. The highest frequencies were observed in **primary care/first contact settings (13 studies)** and **internal medicine (12 studies)**, followed by **dermatology specialized care (10 studies)**, **rheumatology/autoimmune clinics (8 studies)**, **emergency or acute care settings (7 studies)**, and **oncology-related**

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**screening contexts (5 studies).** This distribution highlights that the diagnostic value of dermatology is not confined to specialized environments, but extends across multiple levels of healthcare.

The predominance of primary care and first-contact settings is particularly significant. The reviewed literature consistently emphasizes that many systemic diseases initially manifest with subtle or nonspecific symptoms, while skin findings may be more visible and recognizable at early stages. In this context, clinicians working in primary care are often the first to encounter these signs, making their ability to interpret dermatologic manifestations critical for early diagnosis and appropriate referral. This pattern is especially relevant in healthcare systems where access to specialists may be limited, reinforcing the importance of strong clinical examination skills at the initial level of care [Patel et al., 2021].

Internal medicine appears as the second most represented context, which aligns with the integrative nature of systemic disease management. Internists frequently encounter patients with multisystem involvement, where dermatologic findings can provide important diagnostic clues. The literature supports that skin manifestations in autoimmune diseases, vasculitis, and infectious processes often guide further investigation, including laboratory testing and imaging studies. This explains the high representation of internal medicine in Figure 4, as dermatology and internal medicine are closely interconnected in clinical practice [Rongioletti & Reborá, 2021].

Dermatology specialized care also shows a strong presence, reflecting its role in confirming diagnoses, performing advanced evaluations, and integrating clinical findings with histopathology and immunologic testing. In this setting, dermatologists play a central role in distinguishing between primary cutaneous disorders and systemic diseases with dermatologic manifestations. The reviewed studies indicate that specialized dermatologic assessment enhances diagnostic precision and contributes to multidisciplinary management strategies [Schmidt & Zillikens, 2021].

Rheumatology and autoimmune clinics represent another important context, particularly due to the strong association between skin findings and connective tissue diseases. Conditions such as lupus and dermatomyositis often require close collaboration between dermatologists and rheumatologists, as cutaneous manifestations may reflect disease activity, progression, or response to treatment. The presence of this category in Figure 4 underscores the importance of interdisciplinary approaches in managing complex systemic diseases [Almutairi et al., 2020].

Emergency and acute care settings, although less represented, still demonstrate the relevance of dermatologic findings in urgent clinical scenarios. Infections, drug reactions, vasculitic processes, and thrombotic events may present with acute skin manifestations that require rapid recognition and intervention. The COVID-19 pandemic provided clear examples of how dermatologic signs can appear in acute systemic illness, reinforcing their diagnostic value even in high-pressure clinical environments [Freeman et al., 2020].

Finally, oncology-related contexts appear with the lowest frequency in the figure, but their importance should not be underestimated. Paraneoplastic dermatoses and other malignancy-associated skin findings may serve as early indicators of internal cancer, prompting further investigation. Although fewer studies focused specifically on this context, the literature consistently highlights the potential of dermatology to contribute to oncologic suspicion and early detection [Ferreira et al., 2021].

### Figure 5.

*Distribution of the most frequently reported cutaneous manifestation patterns associated with systemic disease*

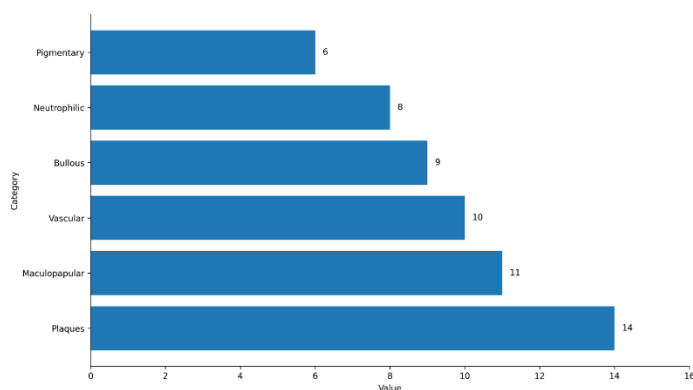


Figure 5 illustrates the distribution of the most commonly reported cutaneous lesion patterns identified across the reviewed literature. The most frequent findings correspond to **inflammatory plaques (14 studies)**, followed by **maculopapular eruptions (11 studies)**, **vascular manifestations such as purpura or livedo (10 studies)**, **vesiculobullous lesions (9 studies)**, **neutrophilic dermatoses (8 studies)**, and **pigmentary alterations (6 studies)**. This distribution highlights that dermatologic morphology is not random but tends to cluster into recognizable patterns that are consistently associated with systemic processes.

Inflammatory plaques represent the most frequently described lesion type, which is consistent with the high representation of chronic inflammatory diseases such as psoriasis and autoimmune dermatoses in the reviewed literature. These lesions are typically characterized by erythema, scaling, and well-demarcated borders, and their presence often reflects sustained immune activation. In systemic conditions, such plaques may indicate ongoing inflammatory signaling pathways that extend beyond the skin, reinforcing their relevance as clinical markers of systemic disease [Gisondi et al., 2020].

Maculopapular eruptions, the second most frequent pattern, are commonly associated with infectious diseases and systemic inflammatory responses. During the COVID-19 pandemic, for example, maculopapular rashes were among the most frequently reported dermatologic findings, often appearing in conjunction with systemic symptoms. Their relatively nonspecific morphology makes them diagnostically challenging; however, their high frequency in systemic conditions explains their prominence in Figure 5 [Freeman et al., 2020].

Vascular manifestations, including purpura and livedoid changes, also occupy a significant position in the figure. These lesions are particularly important because they often reflect underlying vascular injury, endothelial dysfunction, or thrombotic processes. In vasculitis and COVID-19-associated coagulopathy, for instance, such findings have been directly linked to systemic vascular involvement. Their presence may therefore indicate more severe or systemic disease processes, even when cutaneous findings appear localized [Magro et al., 2020; Tolkachjov et al., 2020].

Vesiculobullous lesions represent another important category, often associated with autoimmune blistering diseases such as pemphigoid disorders. These lesions result from autoantibody-mediated damage to structural components of the skin, leading to blister formation. Their diagnostic value lies in their relatively specific morphology and the need for correlation with immunologic and histopathologic findings, which often reveal systemic immune dysfunction [Schmidt & Zillikens, 2021].

Neutrophilic dermatoses, although less frequent, are clinically significant due to their association with systemic inflammatory and neoplastic conditions. Disorders such as Sweet syndrome may present with painful erythematous plaques or nodules and are often linked to underlying infections, inflammatory diseases, or malignancies. Their inclusion in the figure reflects their importance as markers of systemic pathology, even when they are less commonly encountered in general practice [Cohen, 2021].

Pigmentary changes appear as the least represented category in the figure, but they remain relevant in specific systemic contexts. Alterations in skin pigmentation may be associated with endocrine disorders, chronic inflammation, or metabolic conditions. Although less frequently reported in the reviewed studies, their presence can still provide valuable diagnostic clues, particularly when evaluated alongside other clinical findings.

From a descriptive perspective, Figure 5 demonstrates that the **morphological classification of skin lesions remains a fundamental tool for clinical interpretation**, allowing clinicians to categorize and prioritize potential systemic associations. The distribution of lesion types reinforces the importance of pattern recognition in dermatology, as specific morphologies are consistently linked to particular pathophysiological mechanisms and disease categories.

**Figure 6.**

*Geographic distribution of the evidence and representation of international and Latin American contributions*

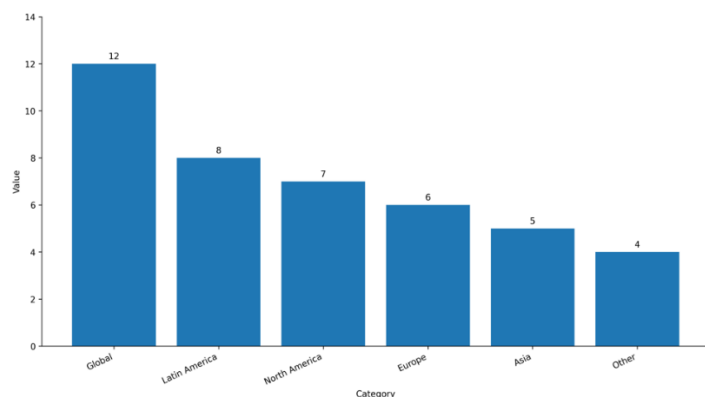


Figure 6 shows the geographic distribution of the evidence included in this review, highlighting a predominance of **global or multi-country studies (12 studies)**, followed by **Latin American contributions—including Mexico, Colombia, and Ecuador (8 studies)**, as well as **North America (7 studies)**, **Europe (6 studies)**, **Asia (5 studies)**, and **other regions (4 studies)**. This distribution demonstrates that the relationship between dermatologic manifestations and systemic disease has been widely studied across different healthcare systems, with meaningful representation from both high-income and middle-income regions.

The predominance of global or multi-country studies reflects the increasing trend toward collaborative research and large-scale data integration, particularly in areas such as infectious diseases, autoimmune conditions, and systemic inflammatory disorders. These studies often provide broader epidemiological perspectives and allow for the identification of consistent clinical patterns across diverse populations. Their prominence in Figure 6 supports the idea that dermatologic manifestations of systemic disease are not region-specific phenomena but rather universal clinical expressions of underlying biological mechanisms [Freeman et al., 2020].

The significant representation of Latin America is particularly relevant for the educational and clinical context of this review. Studies and reviews from Mexico, Colombia, and Ecuador highlight the importance of dermatologic evaluation in settings where access to advanced diagnostic tools may be variable. In these environments, the skin becomes an especially valuable diagnostic resource, as it allows clinicians to identify systemic disease through direct observation and clinical reasoning. The presence of this category in Figure 6 reinforces the applicability of the reviewed evidence to real-world clinical practice in the region, where early recognition of dermatologic signs can improve diagnostic pathways and patient outcomes.

North America and Europe also contribute substantially to the evidence base, reflecting strong research infrastructure and a long-standing tradition of dermatologic and systemic disease research. These regions have produced a significant portion of the literature on autoimmune diseases, vasculitis, and dermatologic manifestations of systemic conditions, often supported by advanced diagnostic technologies and large patient cohorts. Their representation in the figure underscores the role of these regions in shaping current understanding of dermatology as a systemic diagnostic discipline [Schmidt & Zillikens, 2021].

Asian studies, while slightly less represented, provide important contributions, particularly in the areas of infectious diseases, genetic dermatologic conditions, and population-specific clinical patterns. The inclusion of these studies

highlights the global relevance of dermatologic manifestations and the importance of considering geographic and ethnic variability in clinical presentation.

The category of other regions, although the smallest, still contributes to the diversity of the evidence base. This suggests that interest in the systemic implications of dermatologic findings is expanding globally, even in regions with more limited research output.

From a descriptive standpoint, Figure 6 demonstrates that the evidence supporting the diagnostic role of dermatology is **globally distributed**, with meaningful contributions from multiple regions. Importantly, the inclusion of Latin American data confirms that the findings of this review are not limited to high-resource settings but are also applicable to healthcare systems where clinical examination remains a cornerstone of diagnosis.

## DISCUSIÓN

The findings of this review collectively reinforce a central premise: dermatology has evolved from a predominantly descriptive specialty into a **strategic diagnostic discipline that provides clinically actionable insight into systemic disease**. The results demonstrate that cutaneous manifestations are consistently linked to underlying immunologic, inflammatory, vascular, infectious, and neoplastic processes, positioning the skin as a clinically accessible interface through which systemic pathology can be detected, interpreted, and monitored.

One of the most relevant observations emerging from this analysis is the **predominance of immune-mediated and inflammatory mechanisms** as the primary link between dermatologic findings and systemic disease. This is consistent with current scientific understanding, where diseases such as psoriasis, lupus erythematosus, and dermatomyositis are no longer interpreted as isolated cutaneous entities but as systemic conditions with dermatologic expression. The high frequency of these categories in the results supports the growing consensus that immune dysregulation is a unifying pathway across multiple organ systems, with the skin serving as one of its most visible manifestations. This aligns with previous literature highlighting the systemic inflammatory burden associated with dermatologic diseases and their correlation with comorbidities such as cardiovascular disease and metabolic syndrome [Gisondi et al., 2020; Hu & Lan, 2021].

Another important aspect highlighted by the results is the **diagnostic hierarchy of dermatologic contributions**, with early detection occupying the most prominent role. This finding has significant implications for clinical practice and medical education. The ability to recognize early cutaneous signs of systemic disease allows clinicians to initiate timely investigations and referrals, potentially reducing diagnostic delay and improving patient outcomes. This is particularly relevant in conditions where skin findings precede systemic manifestations, such as in lupus or paraneoplastic syndromes. The literature consistently supports the notion that early dermatologic recognition can alter the clinical trajectory of systemic disease, reinforcing the importance of maintaining strong observational skills in clinical training [Patel et al., 2021].

The role of **clinicopathologic correlation** also emerges as a key element in the discussion. Dermatology offers a unique advantage among medical specialties due to the accessibility of the skin for direct examination and biopsy. This allows for the integration of clinical morphology with histopathologic and immunologic data, enhancing diagnostic precision. In diseases such as vasculitis and autoimmune blistering disorders, this correlation is essential for distinguishing between localized and systemic involvement. The results suggest that dermatology not only contributes to suspicion but also to confirmation and classification of systemic disease, bridging bedside observation with laboratory-based diagnosis [Tolkachjov et al., 2020; Schmidt & Zillikens, 2021].

The impact of **infectious diseases, particularly COVID-19**, represents another key point of discussion. The pandemic provided a unique context in which dermatologic manifestations were rapidly studied and correlated with systemic mechanisms such as endothelial injury, complement activation, and thrombotic microangiopathy. The identification of distinct cutaneous patterns associated with varying degrees of disease severity reinforced the concept that the skin can serve as a real-time indicator of systemic pathophysiology. This experience has broadened the clinical perspective of dermatology and highlighted its relevance in acute and critical care settings [Magro et al., 2020; Freeman et al., 2020].

From a clinical perspective, the **morphological classification of lesions** remains a fundamental tool for interpreting systemic associations. The results demonstrate that specific patterns—such as inflammatory plaques, maculopapular eruptions, vascular lesions, and vesiculobullous disorders—are consistently linked to particular pathophysiological mechanisms. This reinforces the importance of pattern recognition as a diagnostic skill, allowing clinicians to narrow differential diagnoses and prioritize investigations. However, the discussion also highlights the need to move beyond purely descriptive approaches, integrating morphology with underlying biological processes to achieve a more comprehensive understanding of disease.

The **geographic distribution of evidence** provides additional insight into the applicability of these findings. While a significant portion of the literature originates from high-resource settings, the inclusion of studies from Latin America demonstrates that the diagnostic value of dermatology is particularly relevant in regions where access to advanced diagnostic tools may be limited. In countries such as Mexico, Colombia, and Ecuador, the ability to identify systemic disease through clinical examination of the skin can serve as a cost-effective and accessible diagnostic strategy. This reinforces the importance of strengthening dermatologic training in these settings and integrating it into primary care and internal medicine practice.

Another key implication of this review is the importance of **interdisciplinary collaboration**. Dermatologic findings often require interpretation within a broader clinical context, involving specialties such as rheumatology, internal medicine, oncology, and infectious disease. The results suggest that dermatology functions as a connecting discipline, facilitating communication between different areas of medicine and contributing to a more holistic approach to patient care. This interdisciplinary perspective is essential for managing complex systemic diseases, where no single specialty can fully address all aspects of the condition.

Despite these strengths, several limitations should be considered. First, as a narrative review, the study relies on the synthesis of existing literature rather than primary data, which may introduce selection bias. Although efforts were made to include high-impact and recent studies, variability in study design, population characteristics, and diagnostic criteria may influence the generalizability of the findings. Additionally, the heterogeneity of dermatologic manifestations and systemic diseases makes it difficult to establish uniform diagnostic algorithms applicable to all clinical scenarios.

Another limitation is the relative underrepresentation of certain regions and disease categories, particularly paraneoplastic and rare dermatologic conditions. While these entities are clinically significant, their lower frequency in the literature may reflect challenges in diagnosis, reporting, or study design. Future research should aim to address these gaps by including more diverse populations and focusing on less common but diagnostically important conditions.

In terms of future directions, this review highlights the need for **prospective and multidisciplinary studies** that further explore the relationship between skin and systemic disease. The integration of dermatology with emerging fields such as molecular medicine, immunology, and artificial intelligence may enhance diagnostic accuracy and enable more personalized approaches to patient care. Additionally, the development of standardized clinical algorithms that incorporate dermatologic findings into systemic evaluation could improve diagnostic efficiency and reduce variability in clinical practice.

## CONCLUSIÓN

This review consolidates current international evidence supporting the concept that dermatology plays a fundamental role in the recognition and interpretation of systemic disease. The findings demonstrate that cutaneous manifestations are not isolated clinical phenomena but rather **integrated expressions of underlying immunologic, inflammatory, vascular, infectious, and neoplastic processes**, making the skin a clinically valuable diagnostic interface.

A central conclusion derived from this analysis is that dermatologic examination contributes significantly to **early detection of systemic disease**, often preceding or complementing internal manifestations. This reinforces the importance of maintaining a strong emphasis on clinical observation and pattern recognition within medical training

and practice. The consistent association between specific lesion morphologies and systemic conditions highlights the reliability of dermatologic findings as diagnostic indicators when interpreted within an appropriate clinical context.

Additionally, the review confirms that dermatology provides a unique advantage through its capacity for **clinicopathologic correlation**, allowing direct integration of visual assessment with histopathological and immunological data. This characteristic enhances diagnostic precision and supports more accurate classification of systemic diseases, particularly in autoimmune, vasculitic, and blistering disorders.

From a clinical systems perspective, the results emphasize that the diagnostic value of dermatology extends across multiple levels of care, including primary care, internal medicine, and specialized services. This broad applicability is especially relevant in healthcare settings where access to advanced diagnostic resources may be limited. In such contexts, including regions like Mexico, Colombia, and Ecuador, the skin represents a **cost-effective and accessible tool for identifying systemic disease**, contributing to improved diagnostic pathways and patient outcomes.

The integration of dermatology into multidisciplinary care models also emerges as a key element. Dermatologic findings frequently serve as a starting point for collaboration with other specialties, facilitating comprehensive evaluation and management of complex conditions. This reinforces the need to view dermatology not as an isolated discipline, but as an essential component of holistic and integrative medicine.

In summary, this review supports the interpretation of the skin as a **visible extension of systemic health**, capable of providing clinically relevant information that enhances diagnostic reasoning, guides investigation, and supports ongoing patient assessment. Strengthening the role of dermatology in both education and clinical practice may contribute to earlier diagnosis, more efficient use of healthcare resources, and improved quality of care at an international level.

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