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CUTANEOUS MANIFESTATIONS OF SYSTEMIC AUTOIMMUNE DISEASES

MANIFESTAÇÕES CUTÂNEAS DAS DOENÇAS AUTOIMUNES SISTÊMICAS

MANIFESTACIONES CUTÁNEAS DE LAS ENFERMEDADES AUTOINMUNES SISTÉMICAS

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ABSTRACT

Introduction: Cutaneous manifestations represent one of the most frequent and clinically informative components of systemic autoimmune diseases, often reflecting complex immune dysregulation that extends beyond the skin. In many autoimmune conditions, dermatological findings may precede systemic involvement, emerge during disease flares, or persist as markers of chronic immune activation. These manifestations provide a visible and accessible interface through which systemic disease activity, severity, and progression may be inferred. As such, careful evaluation of the skin can play a pivotal role in early diagnosis, prognostic stratification, and longitudinal monitoring of patients with systemic autoimmune disorders.

Objective: The primary objective of this systematic review was to comprehensively synthesize contemporary evidence regarding the spectrum and clinical relevance of cutaneous manifestations in systemic autoimmune diseases. Secondary objectives included evaluating the diagnostic value of specific skin phenotypes, assessing their association with systemic organ involvement and disease activity, analyzing their prognostic implications for morbidity and mortality, exploring underlying immunopathological correlations, examining their impact on therapeutic decision-making, and identifying methodological gaps and limitations within the current literature.

Methods: A systematic search was conducted across PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. Predefined inclusion and exclusion criteria were applied, prioritizing studies published within the last five years while allowing extension when necessary to ensure adequate representation. Eligible studies were synthesized qualitatively in accordance with PRISMA recommendations, with structured assessment of risk of bias and certainty of evidence to support an evidence-based interpretation of findings.

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Results and Discussion: Twenty studies met the inclusion criteria, encompassing a broad range of systemic autoimmune diseases, including connective tissue diseases, systemic vasculitides, and overlap syndromes. Across these conditions, specific cutaneous phenotypes consistently correlated with systemic disease activity, internal organ involvement, prognostic outcomes, and patient-reported quality-of-life measures. Skin manifestations such as chronic lupus lesions, dermatomyositis-associated ulcerations, systemic sclerosis-related skin fibrosis, and vasculitic lesions in Sjögren syndrome and systemic vasculitis emerged as clinically meaningful markers of disease severity. Despite consistent trends, heterogeneity in study design, lesion classification, and outcome reporting limited the certainty of evidence in some domains.

Conclusion: The available evidence indicates that cutaneous manifestations are not merely ancillary findings but constitute clinically meaningful markers of systemic autoimmune disease activity and prognosis. Their systematic recognition and interpretation can enhance diagnostic accuracy, facilitate early identification of high-risk patients, and inform individualized management strategies. Integration of structured dermatological assessment into multidisciplinary, evidence-based care models is essential to optimize outcomes and improve quality of life for patients with systemic autoimmune diseases.

Keywords: Autoimmune Diseases. Skin Manifestations. Dermatology. Systemic Disease.

RESUMO

Introdução: As manifestações cutâneas representam um dos componentes mais frequentes e clinicamente informativos das doenças autoimunes sistêmicas, refletindo frequentemente uma complexa desregulação imunológica que se estende além da pele. Em muitas condições autoimunes, os achados dermatológicos podem preceder o acometimento sistêmico, surgir durante exacerbações da doença ou persistir como marcadores de ativação imunológica crônica. Essas manifestações oferecem uma interface visível e acessível por meio da qual a atividade, a gravidade e a progressão da doença sistêmica podem ser inferidas. Dessa forma, a avaliação cuidadosa da pele pode desempenhar um papel fundamental no diagnóstico precoce, na estratificação prognóstica e no monitoramento longitudinal de pacientes com doenças autoimunes sistêmicas.

Objetivo: O objetivo principal desta revisão sistemática foi sintetizar de forma abrangente as evidências contemporâneas sobre o espectro e a relevância clínica das manifestações cutâneas nas doenças autoimunes sistêmicas. Os objetivos secundários incluíram avaliar o valor diagnóstico de fenótipos cutâneos específicos, analisar sua associação com o acometimento de órgãos sistêmicos e a atividade da doença, examinar suas implicações prognósticas para morbidade e mortalidade, explorar correlações imunopatológicas subjacentes, investigar seu impacto na tomada de decisão terapêutica e identificar lacunas metodológicas e limitações na literatura atual.

Métodos: Foi realizada uma busca sistemática nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e na International Clinical Trials Registry Platform. Aplicaram-se critérios de inclusão e exclusão previamente definidos, priorizando estudos publicados nos últimos cinco anos, com extensão do período quando necessário para garantir representatividade adequada. Os estudos elegíveis foram sintetizados qualitativamente de acordo com as recomendações do PRISMA, com avaliação estruturada do risco de viés e da certeza da evidência, a fim de sustentar uma interpretação baseada em evidências.

Resultados e Discussão: Vinte estudos atenderam aos critérios de inclusão, abrangendo uma ampla gama de doenças autoimunes sistêmicas, incluindo doenças do tecido

conjuntivo, vasculites sistêmicas e síndromes de sobreposição. Nessas condições, fenótipos cutâneos específicos correlacionaram-se de forma consistente com a atividade da doença sistêmica, o envolvimento de órgãos internos, os desfechos prognósticos e as medidas de qualidade de vida relatadas pelos pacientes. Manifestações cutâneas como lesões crônicas do lúpus, ulcerações associadas à dermatomiosite, fibrose cutânea relacionada à esclerose sistêmica e lesões vasculíticas na síndrome de Sjögren e nas vasculites sistêmicas emergiram como marcadores clinicamente relevantes de gravidade da doença. Apesar de tendências consistentes, a heterogeneidade no delineamento dos estudos, na classificação das lesões e no relato dos desfechos limitou a certeza da evidência em alguns domínios.

Conclusão: As evidências disponíveis indicam que as manifestações cutâneas não são meros achados acessórios, mas constituem marcadores clinicamente significativos da atividade e do prognóstico das doenças autoimunes sistêmicas. Seu reconhecimento e interpretação sistemáticos podem aprimorar a acurácia diagnóstica, facilitar a identificação precoce de pacientes de alto risco e orientar estratégias de manejo individualizadas. A integração de uma avaliação dermatológica estruturada em modelos de cuidado multidisciplinares e baseados em evidências é essencial para otimizar os desfechos e melhorar a qualidade de vida dos pacientes com doenças autoimunes sistêmicas.

Palavras-chave: Doenças Autoimunes. Manifestações Cutâneas. Dermatologia. Doença Sistêmica.

RESUMEN

Introducción: Las manifestaciones cutáneas representan uno de los componentes más frecuentes y clínicamente informativos de las enfermedades autoinmunes sistémicas, reflejando a menudo una compleja desregulación inmunológica que se extiende más allá de la piel. En muchas condiciones autoinmunes, los hallazgos dermatológicos pueden preceder al compromiso sistémico, surgir durante los brotes de la enfermedad o persistir como marcadores de activación inmunológica crónica. Estas manifestaciones proporcionan una interfaz visible y accesible a través de la cual pueden inferirse la actividad, la gravedad y la progresión de la enfermedad sistémica. Por lo tanto, la evaluación cuidadosa de la piel puede desempeñar un papel clave en el diagnóstico precoz, la estratificación pronóstica y el seguimiento longitudinal de los pacientes con enfermedades autoinmunes sistémicas.

Objetivo: El objetivo principal de esta revisión sistemática fue sintetizar de manera integral la evidencia contemporánea sobre el espectro y la relevancia clínica de las manifestaciones cutáneas en las enfermedades autoinmunes sistémicas. Los objetivos secundarios incluyeron evaluar el valor diagnóstico de fenotipos cutáneos específicos, analizar su asociación con el compromiso de órganos sistémicos y la actividad de la enfermedad, examinar sus implicaciones pronósticas en la morbilidad y la mortalidad, explorar correlaciones inmunopatológicas subyacentes, analizar su impacto en la toma de decisiones terapéuticas e identificar vacíos metodológicos y limitaciones en la literatura actual.

Métodos: Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y en la International Clinical Trials Registry Platform. Se aplicaron criterios de inclusión y exclusión previamente definidos, priorizando estudios publicados en los últimos cinco años, con extensión del período cuando fue necesario para asegurar una representación adecuada. Los estudios elegibles se sintetizaron cualitativamente de acuerdo con las recomendaciones PRISMA, con una evaluación estructurada del riesgo de sesgo y de la certeza de la evidencia, con el fin de respaldar una interpretación basada en la evidencia.

Resultados y Discusión: Veinte estudios cumplieron los criterios de inclusión, abarcando una amplia gama de enfermedades autoinmunes sistémicas, incluidas enfermedades del tejido conectivo, vasculitis sistémicas y síndromes de superposición. En estas condiciones, fenotipos cutáneos específicos se correlacionaron de manera consistente con la actividad de la enfermedad sistémica, el compromiso de órganos internos, los resultados pronósticos y las medidas de calidad de vida informadas por los pacientes. Manifestaciones cutáneas como las lesiones crónicas del lupus, las ulceraciones asociadas a la dermatomiositis, la fibrosis cutánea relacionada con la esclerosis sistémica y las lesiones vasculíticas en el síndrome de Sjögren y en las vasculitis sistémicas surgieron como marcadores clínicamente relevantes de la gravedad de la enfermedad. A pesar de las tendencias consistentes, la heterogeneidad en el diseño de los estudios, la clasificación de las lesiones y el reporte de los resultados limitó la certeza de la evidencia en algunos dominios.

Conclusión: La evidencia disponible indica que las manifestaciones cutáneas no son hallazgos accesorios, sino marcadores clínicamente significativos de la actividad y el pronóstico de las enfermedades autoinmunes sistémicas. Su reconocimiento e interpretación sistemáticos pueden mejorar la precisión diagnóstica, facilitar la identificación temprana de pacientes de alto riesgo e informar estrategias de manejo individualizadas. La integración de una evaluación dermatológica estructurada en modelos de atención multidisciplinarios y basados en la evidencia es esencial para optimizar los resultados y mejorar la calidad de vida de los pacientes con enfermedades autoinmunes sistémicas.

Palabras clave: Enfermedades Autoinmunes. Manifestaciones Cutáneas. Dermatología. Enfermedad Sistémica.

1 INTRODUCTION

Systemic autoimmune diseases comprise a heterogeneous group of conditions characterized by immune dysregulation and multisystem involvement, with the skin representing one of the most frequently affected organs[1]. Cutaneous findings may precede systemic manifestations, occur concurrently, or emerge as markers of disease flares, offering an accessible window into underlying immune activity[1]. In many autoimmune disorders, dermatological signs are among the earliest clinical clues prompting further diagnostic investigation and specialist referral[1]. The high prevalence and diversity of skin involvement underscore the importance of recognizing these manifestations within a systemic clinical framework[2].

The skin acts not only as a target organ but also as an active immunological interface, reflecting complex interactions between innate and adaptive immune responses[2]. Autoimmune-mediated inflammation in the skin is often driven by autoantibody deposition, immune complex formation, and cytokine-mediated tissue injury[2]. These mechanisms contribute to a wide spectrum of lesions, ranging from nonspecific rashes to highly characteristic patterns that may suggest a specific systemic diagnosis[3]. Consequently, detailed dermatological evaluation can significantly narrow differential diagnoses in patients with suspected autoimmune disease[3].

Classic examples such as malar rash in systemic lupus erythematosus, heliotrope rash in dermatomyositis, and sclerodactyly in systemic sclerosis illustrate the diagnostic value of cutaneous signs[3]. These manifestations often correlate with internal organ involvement, disease severity, and long-term prognosis[4]. In some cases, skin findings may serve as predictors of complications such as interstitial lung disease, renal involvement, or malignancy[4]. Understanding these associations is therefore critical for comprehensive patient assessment and risk stratification[4].

Beyond diagnosis, cutaneous manifestations may reflect disease activity and response to therapy, providing a noninvasive means of monitoring systemic autoimmune conditions[5]. Improvement or worsening of skin lesions often parallels changes in systemic inflammation and immunological markers[5]. However, treatment-related skin changes, including drug-induced eruptions or infections secondary to immunosuppression, may confound clinical interpretation[5]. Differentiating disease-related lesions from therapy-associated findings remains a frequent clinical challenge[6].

The heterogeneity of skin involvement across autoimmune diseases is compounded by overlapping clinical patterns and shared pathogenic pathways[6]. Similar cutaneous phenotypes may be observed in distinct autoimmune conditions, complicating diagnosis in

early or atypical presentations[6]. Moreover, ethnic background, genetic predisposition, and environmental factors can influence the expression and severity of dermatological manifestations[7]. These variables contribute to significant interindividual variability in clinical presentation and disease course[7].

Recent advances in immunodermatology have expanded understanding of the molecular and cellular mechanisms underlying autoimmune skin disease[7]. Novel insights into cytokine networks, interferon signatures, and immune cell trafficking have clarified links between cutaneous and systemic inflammation[8]. These discoveries have also facilitated the development of targeted therapies that may improve both skin and systemic outcomes[8]. Nevertheless, evidence regarding the clinical utility of skin findings in guiding management decisions remains fragmented[8].

Systematic synthesis of current literature is essential to clarify the diagnostic, prognostic, and therapeutic relevance of cutaneous manifestations in systemic autoimmune diseases[9]. Previous narrative reviews have often focused on single diseases or specific lesion types, limiting broader clinical applicability[9]. A comprehensive systematic approach allows comparison across conditions, identification of consistent patterns, and evaluation of evidence quality[9]. Such analysis is particularly relevant for multidisciplinary teams managing complex autoimmune patients[10].

Despite growing interest in this field, gaps persist regarding standardized classification of lesions, outcome reporting, and integration of dermatological findings into clinical algorithms[10]. Variability in study design and assessment tools hampers direct comparison between studies[10]. Addressing these limitations through rigorous evidence synthesis may support more consistent clinical practice and inform future research priorities[11]. Ultimately, improved understanding of cutaneous manifestations has the potential to enhance early diagnosis, personalize treatment, and optimize long-term outcomes in systemic autoimmune diseases[11].

2 OBJECTIVES

The main objective of this systematic review was to comprehensively evaluate the spectrum, clinical relevance, and diagnostic implications of cutaneous manifestations associated with systemic autoimmune diseases. The secondary objectives were to analyze the correlation between specific skin findings and systemic organ involvement, to assess the prognostic value of dermatological manifestations in disease activity and outcomes, to explore underlying immunopathological mechanisms linking skin and systemic disease, to evaluate therapeutic implications of cutaneous involvement in guiding management

strategies, and to identify gaps and methodological limitations in the current literature to inform future research directions.

3 METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, following a predefined protocol designed to ensure methodological rigor and reproducibility. A comprehensive literature search was performed using PubMed, Scopus, Web of Science, the Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. The search strategy combined controlled vocabulary and free-text terms related to systemic autoimmune diseases and cutaneous manifestations, adapted for each database to maximize sensitivity.

Studies were eligible for inclusion if they evaluated skin manifestations in patients with systemic autoimmune diseases, including but not limited to systemic lupus erythematosus, dermatomyositis, systemic sclerosis, Sjögren syndrome, and vasculitides. The primary time window was limited to the last five years, with expansion up to ten years when fewer than ten eligible studies were identified for a specific condition. Human studies were prioritized, while relevant animal or in vitro studies were documented separately and considered only for mechanistic context. No language restrictions were applied, and studies with small sample sizes were included but explicitly recognized as a limitation.

Study selection was performed independently by two reviewers, who screened titles and abstracts followed by full-text assessment of potentially eligible articles. Discrepancies were resolved by consensus or consultation with a third reviewer when necessary. Data extraction was conducted using standardized forms, capturing information on study design, population characteristics, autoimmune diagnosis, type of cutaneous manifestations, outcomes assessed, and main conclusions. Duplicate extraction was performed to minimize errors and ensure data accuracy.

Risk of bias was assessed using appropriate tools according to study design, including the Cochrane Risk of Bias 2 tool for randomized studies, ROBINS-I for non-randomized studies, and QUADAS-2 for diagnostic accuracy studies. The certainty of evidence for key outcomes was evaluated using the Grading of Recommendations Assessment, Development and Evaluation approach. A systematic review design was justified due to the clinical heterogeneity and expanding volume of literature in this field, aiming to provide an integrated and evidence-based synthesis relevant to multidisciplinary clinical practice.

4 RESULTS

A total of 20 studies met the inclusion criteria and were included in the final qualitative synthesis.

Table 1

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Marzano AV et al., 2020	Patients with systemic lupus erythematosus and cutaneous involvement	Cutaneous phenotypes, systemic activity, immunological markers	Cutaneous manifestations were strongly associated with systemic disease activity and serological abnormalities.
Fiorentino D et al., 2020	Patients with classic and amyopathic dermatomyositis	Skin patterns, malignancy occurrence	Specific cutaneous features were linked to an increased risk of associated malignancy.
Ingegnoli F et al., 2020	Cohort of patients with systemic sclerosis	Skin thickness score, visceral involvement	Greater extent of skin involvement predicted internal organ complications.
Boniface K et al., 2021	Patients with autoimmune connective tissue diseases	Cutaneous cytokine expression profiles	Shared inflammatory pathways connected skin involvement with systemic autoimmunity.
Trovato E et al., 2021	Patients with primary Sjögren syndrome	Cutaneous vasculitis, systemic severity	Vasculitic skin lesions were associated with more severe systemic disease.
Chasset F et al., 2021	Patients across the lupus erythematosus spectrum	Cutaneous subtypes, clinical outcomes	Distinct cutaneous subtypes showed different prognostic and systemic profiles.
Paolino G et al., 2021	Patients with mixed connective tissue disease	Dermatological manifestations, diagnostic utility	Skin findings contributed to earlier recognition of overlap syndromes.
Hernández-Molina G et al., 2022	Patients with systemic autoimmune vasculitis	Purpura, ulcers, necrosis, systemic involvement	Cutaneous vasculitis reflected the extent of systemic vascular disease.
Fania L et al., 2022	Patients with dermatomyositis and polymyositis	Skin lesions, myositis-specific autoantibodies	Certain cutaneous lesions correlated with specific autoantibody profiles.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Kubo S et al., 2022	Patients with systemic sclerosis	Digital ulcers, survival outcomes	Ischemic digital lesions were associated with poorer survival.
Maldonado F et al., 2022	Lupus patients receiving immunosuppressive therapy	Skin flares, therapeutic response	Cutaneous disease activity paralleled systemic treatment response.
Marques CDL et al., 2023	Patients with rheumatoid arthritis and extra-articular disease	Rheumatoid nodules, vasculitis	Skin involvement indicated more aggressive systemic disease.
Hesselstrand R et al., 2023	Patients with early systemic sclerosis	Skin biomarkers, disease progression	Early cutaneous changes predicted subsequent systemic progression.
Ruffatti A et al., 2023	Patients with antiphospholipid syndrome	Livedo reticularis, thrombotic events	Cutaneous signs were associated with increased thrombotic risk.
Feng R et al., 2023	Patients with connective tissue diseases	Nailfold capillaroscopic alterations	Microvascular skin changes correlated with systemic involvement.
Cafaro G et al., 2024	Patients with primary Sjögren syndrome	Cutaneous vasculitis, lymphoma development	Skin vasculitis predicted higher risk of lymphoproliferative disease.
Zhang X et al., 2024	Dermatomyositis cohorts	Cutaneous severity scores, lung involvement	Severe skin disease was associated with interstitial lung disease.
Marzano AV et al., 2024	Patients with autoimmune and autoinflammatory overlap syndromes	Neutrophilic dermatoses, systemic activity	Cutaneous phenotypes reflected underlying systemic immune dysregulation.
Patel P et al., 2024	Patients with systemic lupus erythematosus	Chronic cutaneous lesions, organ damage	Persistent skin disease was linked to cumulative systemic damage.
Tani C et al., 2024	Patients with connective tissue diseases	Patient-reported skin outcomes, quality of life	Cutaneous involvement significantly impaired quality of life.

5 RESULTS AND DISCUSSION

The studies included in this review demonstrated that cutaneous manifestations are highly prevalent across systemic autoimmune diseases and frequently represent an early or sentinel sign of systemic involvement[12]. In cohorts of systemic lupus erythematosus, dermatomyositis, and systemic sclerosis, skin lesions were often the initial feature leading to diagnosis and subsequent organ evaluation[12]. These findings reinforce the concept that dermatological assessment plays a central role in the diagnostic pathway of autoimmune diseases[12].

Marzano and colleagues reported that distinct cutaneous phenotypes in systemic lupus erythematosus were significantly associated with systemic disease activity and immunological markers[13]. Their findings highlighted correlations between chronic cutaneous lesions and higher cumulative organ damage scores[13]. This association supports the prognostic relevance of persistent skin involvement beyond cosmetic or localized disease considerations[13].

In dermatomyositis, Fiorentino et al. demonstrated that specific cutaneous patterns, particularly ulcerative and necrotic lesions, were linked to an increased risk of underlying malignancy[14]. Zhang and collaborators further confirmed that greater cutaneous severity was associated with interstitial lung disease, a major determinant of morbidity and mortality[14]. Together, these studies suggest that skin findings in dermatomyositis may act as clinical markers of systemic severity and complication risk[14].

Systemic sclerosis studies consistently showed that the extent of skin involvement correlates with visceral disease and survival outcomes[15]. Ingegnoli et al. observed that higher skin thickness scores were predictive of internal organ involvement, while Kubo et al. identified digital ulcers as markers of poorer prognosis[15]. These results emphasize the value of skin assessment in staging disease severity and guiding follow-up intensity[15].

In primary Sjögren syndrome, Trovato and Cafaro independently reported that cutaneous vasculitis was associated with more severe systemic disease and increased lymphoma risk[16]. These findings underscore the importance of recognizing vasculitic skin lesions as red flags warranting closer systemic surveillance[16]. The prognostic implications of such lesions extend beyond glandular involvement and dryness symptoms[16].

Autoimmune vasculitides and antiphospholipid syndrome studies highlighted that purpura, ulcers, livedo reticularis, and necrosis reflect systemic vascular pathology[17]. Hernández-Molina and Ruffatti demonstrated strong associations between these cutaneous signs and thrombotic or multi-organ vascular involvement[17]. These manifestations therefore provide clinically accessible indicators of underlying systemic vascular risk[17].

Overlap syndromes and mixed connective tissue disease present particular diagnostic challenges due to shared features across conditions[18]. Paolino and Marzano showed that specific dermatological patterns, including neutrophilic dermatoses, may help differentiate overlap syndromes and reflect immune dysregulation[18]. Such findings support the integration of dermatological expertise into multidisciplinary autoimmune clinics[18].

Mechanistic studies revealed shared inflammatory pathways linking skin and systemic autoimmunity[19]. Boniface and Feng demonstrated that cytokine profiles and microvascular alterations observed in the skin paralleled systemic immune activation[19]. These data provide biological plausibility for the observed clinical correlations and support skin-targeted biomarkers as surrogates of systemic disease activity[19].

From a patient-centered perspective, Tani et al. highlighted that cutaneous involvement significantly impairs quality of life across connective tissue diseases[20]. Skin symptoms contributed to physical discomfort, psychological distress, and social limitations independent of internal organ disease[20]. These findings emphasize the need to address dermatological manifestations as a core component of holistic autoimmune care[20].

Despite consistent associations, the overall certainty of evidence ranged from low to moderate due to observational designs, heterogeneous outcome measures, and limited longitudinal data[21]. GRADE assessment revealed stronger confidence for prognostic associations in systemic sclerosis and dermatomyositis compared with other conditions[21]. Future well-designed prospective studies are required to standardize lesion classification and clarify causal relationships[21].

6 CONCLUSION

The present systematic review demonstrated that cutaneous manifestations are common, clinically significant features of systemic autoimmune diseases and frequently serve as early indicators of systemic involvement. Across multiple conditions, specific skin phenotypes were consistently associated with disease activity, internal organ complications, and long-term outcomes. The evidence supports the concept that the skin reflects underlying immune dysregulation rather than isolated organ involvement. Recognition of these patterns can therefore contribute meaningfully to comprehensive disease assessment.

From a clinical perspective, dermatological findings should be regarded as integral components of autoimmune disease evaluation rather than secondary or cosmetic concerns. Skin manifestations may guide diagnostic reasoning, inform prognostic stratification, and prompt timely investigation for systemic complications such as malignancy, vascular disease, or interstitial lung involvement. Incorporating structured dermatological assessment into

routine care may improve early detection and monitoring strategies. Multidisciplinary collaboration between dermatology, rheumatology, immunology, and internal medicine is essential to optimize patient outcomes.

The existing literature is limited by heterogeneity in study design, lesion classification, and outcome reporting. Most available data derive from observational studies with variable follow-up durations, limiting causal inference and long-term prognostic conclusions. Small sample sizes and disease-specific cohorts further restrict generalizability. These limitations contributed to low to moderate certainty of evidence for several outcomes.

Future research should prioritize prospective, multicenter studies using standardized definitions and validated skin severity indices. Integration of dermatological findings with immunological biomarkers, imaging data, and patient-reported outcomes may clarify mechanistic links and enhance risk prediction models. Additionally, interventional studies evaluating whether targeted treatment of skin disease modifies systemic outcomes would provide clinically actionable evidence.

In conclusion, cutaneous manifestations represent valuable clinical markers in systemic autoimmune diseases, offering insights into diagnosis, prognosis, and disease activity. An evidence-based, multidisciplinary, and individualized approach to skin involvement is essential to advance patient care. Systematic integration of dermatological expertise into autoimmune disease management has the potential to improve diagnostic accuracy, personalize therapy, and enhance quality of life for affected patients.

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