

CUTANEOUS LUPUS CORRELATION BETWEEN DERMATOLOGICAL MANIFESTATIONS AND SYSTEMIC ACTIVITY

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ABSTRACT

Morbidity Lupus erythematosus is an autoimmune pathology whose clinical spectrum ranges from isolated cutaneous manifestations to severe multivisceral systemic involvement. This study aimed to analyze the interdependence between specific and nonspecific dermatological phenotypes and systemic inflammatory activity in lupus. An integrative literature review was conducted, designed according to the PRISMA protocol guidelines, through a systematized search in the PubMed, Scopus, and SciELO databases. Following the application of rigorous eligibility criteria focused on original studies published in the last decade, nine articles were selected for qualitative synthesis. The evidence indicates that the skin acts as a sentinel organ in the disease course. A predictive risk hierarchy was observed: acute cutaneous lupus and nonspecific lesions, such as vasculitis and alopecia, are strongly associated with systemic exacerbation, reflected by high clinical scores (such as Mex-SLEDAI), anti-dsDNA positivity, and complement consumption. The subacute subtype denotes intermediate systemic activity, strongly correlated with anti-Ro/SSA antibodies and photosensitivity. Conversely, chronic presentations predominantly reflect accumulated, irreversible tissue damage, requiring clinical distinction from current inflammatory activity using validated indices like CLASI. It is concluded that the detailed characterization of the dermatological phenotype constitutes an essential clinical biomarker, indispensable for risk stratification, anticipating visceral involvement, and individualizing therapeutics in the management of lupus patients.

Keywords: Autoimmunity, Biomarkers, Cutaneous manifestations, Diagnosis, Systemic lupus erythematosus.

INTRODUCTION

Lupus erythematosus (LE) comprises a heterogeneous group of chronic inflammatory autoimmune diseases, with a spectrum ranging from strictly cutaneous manifestations to severe multivisceral systemic involvement.¹⁻³ The skin is the second most frequently affected system in systemic lupus erythematosus (SLE), occurring in 70% to 85% of patients and representing the initial symptom in up to 25% of cases.^{1,2,4} Fijałkowska, Kądziała, and Żebrowska¹ highlight that clinical diversity and similarity to other dermatoses may delay diagnosis, making the identification of cutaneous lesions a valuable diagnostic tool.¹

Although the mechanistic relationship between cutaneous lupus erythematosus (CLE) and the systemic form is not fully understood, Maz and Kahlenberg⁴ emphasize that both presentations share common pathways of immune activation, particularly those mediated by type I interferon (IFN) and autoreactive lymphocytes.^{2,4} Clinically, the Gilliam and Sontheimer classification subdivides lesions into LE-specific and LE-nonspecific lesions.^{1,2,5}

Specific manifestations are categorized as acute (ACLE), subacute (SCLE), and chronic (CCLE).^{1,2,5,6} Filotico and Mastrandrea⁵ note that this subdivision reflects a clinical and histological polarity, in which chronicity and greater cutaneous involvement often correspond to a lower immediate risk of progression to SLE.⁵ In contrast, nonspecific lesions, such as vasculitis, Raynaud phenomenon, and nonscarring alopecia, frequently correlate with periods of systemic disease activity and a higher risk of internal organ damage.^{3,5,7,8}

Elmgren and Nyberg⁶ reinforce that clinical surveillance during the first years after a diagnosis of CLE is crucial, given the higher risk of systemic progression during this period⁶. The pathogenesis of CLE is influenced by genetic and hormonal factors as well as environmental triggers, with ultraviolet (UV) radiation being the main inducer and exacerbating factor of lesions.^{1,2,4,6} Vale and Garcia² state that sun exposure induces keratinocyte apoptosis and the production of pro-inflammatory cytokines, triggering the recruitment of plasmacytoid dendritic cells (pDCs), which are major producers of IFN.^{2,4,9}

Brahmanti, Wahono, Pratama, Rahman, Suhendra, Rizky, and Mukti⁸ demonstrated that patients with cutaneous manifestations have significantly higher scores on the disease activity index (Mex-SLEDAI), suggesting that the skin acts as a reliable biomarker of systemic inflammation.^{7,8} The morbidity associated with cutaneous lupus is substantial, severely affecting quality of life because of the disfiguring potential of sequelae such as scarring and alopecia.^{1,3,6,7} Childs and Merola⁷ point out that, although antimalarials are the cornerstone of systemic therapy, the evolution toward biologic therapies and small molecules reflects the need for more precise and safer management.⁷

Ker, Teske, Feng, Chong, and Werth⁹ emphasize that the early identification of predictive factors, using validated instruments such as the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), allows timely interventions to minimize irreversible sequelae.^{6,9} Given this complexity, the present article aims to analyze the interdependence between specific and nonspecific dermatological manifestations and systemic disease activity in lupus. It seeks to provide a theoretical and clinical basis to support the identification of cutaneous patterns that may precede or indicate worsening internal involvement, thereby optimizing patient management and prognosis.

OBJECTIVES

To General objective

To analyze the correlation between the dermatological manifestations of cutaneous lupus and systemic disease activity, considering the different clinical subtypes and their association with laboratory markers and systemic manifestations.

Specific Objectives

- Identify and describe the main dermatological manifestations of cutaneous lupus, including their clinical classifications (acute, subacute, and chronic).
- Evaluate the association between the different subtypes of cutaneous lupus and the levels of systemic disease activity.

- Correlate specific cutaneous manifestations, such as malar rash, discoid lesions, and photosensitivity, with laboratory markers of disease activity, including autoantibodies and complement levels.
- Investigate the relationship between dermatological manifestations and systemic organ involvement in systemic lupus erythematosus.
- Compare the prognostic potential of different cutaneous manifestations in predicting systemic disease activity.

METHODS

This is an integrative literature review with a descriptive design and qualitative approach, conducted with the aim of analyzing and synthesizing scientific knowledge regarding the correlation between dermatological manifestations and systemic activity in lupus erythematosus. To ensure methodological rigor and transparency, the study selection process was structured in accordance with the recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol.

The literature search was conducted systematically in three electronic health databases: PubMed (via the National Library of Medicine), Scopus (Elsevier), and SciELO (Scientific Electronic Library Online). The search strategy was developed by combining controlled health descriptors (DeCS and MeSH) with Boolean operators. The search string was established using the terms “Lupus Erythematosus” AND “Cutaneous” AND “Disease Activity” AND “Systemic Skin Manifestations,” ensuring the simultaneous intersection of all concepts within the same publication. In the Scopus and SciELO databases, the syntax was adapted according to the filters and specific characteristics of each platform.

To define the sample, rigorous eligibility criteria aligned with the guiding research question were established. Original articles were included, comprising observational studies, cohort studies, case-control studies, and clinical trials that primarily investigated the clinical, laboratory, or prognostic correlation between cutaneous lesions and systemic disease involvement. Publications were also required to fall within the previous ten years, be available in full text free of charge, be written in Portuguese, English, or Spanish, and exclusively report research conducted in humans.

In contrast, exclusion criteria included articles duplicated across databases, as well as study designs with a low level of evidence or without clear methodological description, such as narrative reviews, case reports, and case series with small samples. Editorials, letters to the editor, preliminary reports, abstracts published in conference proceedings, in vitro studies or experimental animal studies, as well as studies focused strictly on topical treatment of cutaneous lupus without establishing a correlation with overall systemic activity, were also excluded.

The process of study identification, screening, and selection was conducted in consecutive and documented stages, as presented in Figure 1. The initial search of the databases identified 256 publications, of which 166 were retrieved from PubMed, 62 from Scopus, and 28 from SciELO. During the identification stage, 56 articles were immediately excluded as duplicates. The remaining 200 records underwent primary screening through independent and careful review of titles and abstracts, during which 165 manuscripts were excluded because they did not address the thematic scope or met the pre-established exclusion criteria.

Subsequently, the 35 articles considered potentially eligible were retrieved and assessed in full text. After this in-depth analysis, 26 studies were excluded for specific reasons, such as incompatible study design or absence of clear correlational data. Following rigorous application of all methodological criteria, the final sample consisted of nine articles.

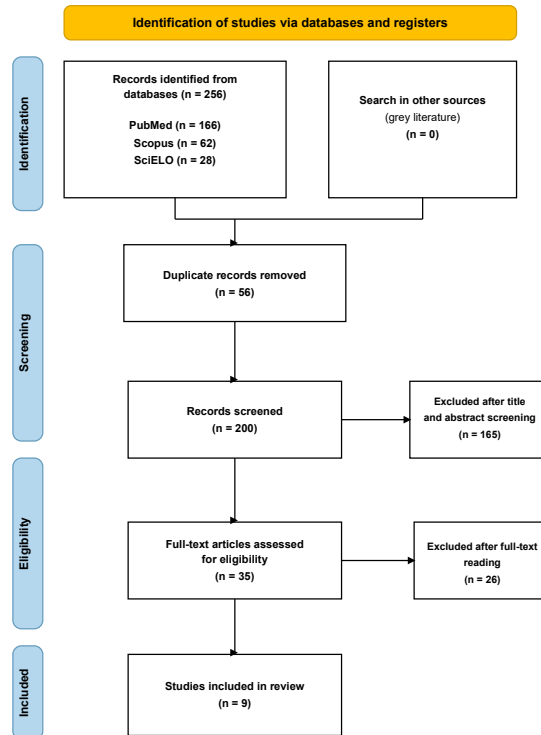


Figure 1: Flowchart of the Selection of Studies Included in the Integrative Review
Source: Prepared by the authors, 2026.

RESULTS AND DISCUSSIONS

The integrated analysis of the selected studies demonstrates that cutaneous lupus should not be understood merely as an isolated dermatological manifestation, but rather as the clinical expression of an immunoinflammatory spectrum that may range from disease restricted to the skin to forms associated with significant systemic activity. This interpretation is essential to the present study, since the correlation between dermatological manifestations and systemic activity depends not only on the presence or absence of cutaneous lesions, but also on the clinical subtype, extent of the lesions, association with nonspecific manifestations, serological profile, and coexistence of systemic signs.

The cutaneous manifestations of lupus erythematosus are generally classified as specific and nonspecific lesions. Specific lesions are those in which clinical and histopathological findings support the diagnosis of cutaneous lupus, including acute cutaneous lupus, subacute cutaneous lupus, and chronic cutaneous lupus. This classification, originally proposed by Gilliam and Sontheimer, remains the most widely used in clinical practice and in the literature, although it has limitations, particularly because of clinical overlap among subtypes and the absence of universally accepted diagnostic criteria for all forms of cutaneous lupus.¹⁻³ This classificatory limitation is relevant because different cutaneous subtypes show distinct patterns in relation to

systemic activity: while acute cutaneous lupus tends to accompany more evident systemic activity, localized discoid lupus frequently behaves as predominantly cutaneous disease.¹⁻⁵

Across the articles analyzed, there was convergence regarding the high frequency of cutaneous manifestations in systemic lupus erythematosus. Recent reviews indicate that dermatological changes occur in approximately 70% to 85% of patients with systemic lupus erythematosus during the course of the disease and may constitute the initial manifestation in up to one quarter of cases.^{2,5} This finding reinforces the concept that the skin functions as a sentinel organ in lupus, since it may signal systemic immune activity even before the development of severe organ manifestations. However, clinical interpretation requires caution: not every cutaneous lesion in a patient with lupus indicates severe systemic activity, and not every form of cutaneous lupus progresses to systemic lupus. The central contribution of the literature lies precisely in distinguishing which dermatological patterns have greater prognostic value.

Acute cutaneous lupus is the subtype most closely associated with active systemic lupus erythematosus. Its classic manifestation is the malar rash, characterized by symmetrical erythema over the malar region and bridge of the nose, usually sparing the nasolabial folds, with a predilection for photoexposed areas.^{1,2,5} This manifestation has diagnostic and prognostic importance because it is included in the classification criteria for systemic lupus and is associated with periods of inflammatory exacerbation. In the 2019 European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR) criteria, the mucocutaneous domain assigns different scores to cutaneous manifestations, with acute cutaneous lupus receiving a higher score than discoid or subacute lupus, reflecting its greater weight as an expression of systemic disease.^{2,5}

The association between malar rash and systemic activity was reinforced by the cross-sectional study by Brahmanti, Wahono, Pratama, Rahman, Suhendra, Rizky, and Mukti⁸, in which patients with malar rash had significantly higher Mex-SLEDAI scores than patients without this manifestation. In this study, malar rash was present in 20.4% of the evaluated patients and was associated with greater disease activity, with a median Mex-SLEDAI score of 8 in patients with malar rash versus 2 in those without this manifestation.⁸ This finding is particularly relevant because it provides quantitative evidence for an association frequently described clinically: malar rash is not merely an aesthetic or diagnostic finding, but may reflect a state of greater systemic activation.

From an immunological perspective, this association is biologically plausible. Acute cutaneous lupus is related to immune complex deposition, complement activation, increased keratinocyte apoptosis, and an exacerbated response to ultraviolet radiation.¹⁻³ Ultraviolet radiation promotes cellular damage, exposure of nuclear autoantigens, and alterations in inflammatory pathways, favoring autoantibody production and amplification of the immune response. Thus, the skin not only reflects systemic activity but may also participate in the immunopathogenic cycle that perpetuates the disease. This interpretation helps explain why photoinduced manifestations, such as malar rash and photosensitivity, frequently accompany periods of greater activity.

Subacute cutaneous lupus occupies an intermediate position in this correlation. Clinically, it presents with annular, polycyclic, or papulosquamous lesions, predominantly in photoexposed areas, with less tendency to scar than discoid lupus but with a strong association with photosensitivity and anti-Ro/SSA antibodies.^{1,2,7} The literature indicates that a significant proportion of patients with subacute cutaneous lupus may meet classification criteria for systemic lupus, although often with milder systemic manifestations, such as arthralgia, myalgia, and constitutional symptoms.¹ This distinction is crucial: SCLL does not necessarily indicate severe systemic disease, but it suggests a greater likelihood of systemic autoimmunity compared with localized discoid lupus.

In the study by Brahmanti, Wahono, Pratama, Rahman, Suhendra, Rizky, and Mukti⁸, subacute cutaneous lupus was observed in 11.1% of patients and showed one of the strongest correlations with systemic activity, with a median Mex-SLEDAI score of 9 in patients with SCLE versus 2 in those without SCLE, with statistical significance.⁸ In addition, SCLE was associated with malar rash, vasculitis, and fatigue, suggesting that its presence may identify patients with a more inflammatory phenotype and a greater systemic burden.⁸ This association should not be interpreted as direct causality, since the cross-sectional design limits temporal inferences; nevertheless, the finding strengthens the hypothesis that SCLE, particularly when coexisting with nonspecific lesions or systemic symptoms, should prompt a broader clinical and laboratory investigation.

The strong relationship between SCLE and anti-Ro/SSA also has relevant implications. Vale and Garcia² highlight that anti-Ro/SSA is present in a large proportion of SCLE cases and is associated with the marked photosensitivity of this subtype, while anti-La/SSB may coexist less frequently². This information allows two distinct axes of correlation to be identified: in ACLE, systemic activity is often linked to anti-dsDNA, hypocomplementemia, and overall SLE activity; in SCLE, the correlation is more strongly related to anti-Ro/SSA, photosensitivity, and generally less aggressive systemic manifestations.² Therefore, the mere presence of a cutaneous lesion is not sufficient; the dermatological subtype must be interpreted together with the serological profile.

Chronic cutaneous lupus, particularly discoid lupus, behaves differently. Discoid lesions are chronic erythematous-squamous plaques, usually located on the face, scalp, and ears, with the potential to progress to atrophy, dyspigmentation, and scarring.^{2,5,7} This subtype is most strongly associated with permanent cutaneous damage, but not necessarily with greater systemic activity. Localized discoid lupus usually remains confined to the skin, whereas generalized, extensive, or progressive forms may carry a higher risk of association with SLE.⁵ This distinction is essential to avoid two clinical errors: underestimating patients with generalized discoid lupus while, at the same time, overestimating systemic risk in every patient with localized discoid lesions.

The review by Stull, Sprow, and Werth³ reinforces this prognostic gradation by indicating that patients with localized discoid lupus, tumid lupus, lupus profundus, and hypertrophic forms tend to have disease more limited to the skin, whereas patients with generalized discoid lupus, SCLE, ACLE, or nonspecific lesions are more likely to have associated systemic disease³. The same study highlights that progression from cutaneous lupus to systemic lupus occurs in a minority of patients, but in a clinically relevant proportion, with cumulative incidence increasing over the years.³ This supports an important practical conclusion: cutaneous lupus requires longitudinal follow-up, even when initially restricted to the skin.

This interpretation is consistent with the findings of Fijałkowska, Kądziała, and Żebrowska¹, who describe a risk of progression to SLE in the years following a diagnosis of cutaneous lupus and emphasize the need to assess internal organs before considering the condition exclusively dermatological¹. This recommendation has a direct impact on the present topic, since the correlation between the skin and systemic activity is not limited to the time of diagnosis. It may emerge during follow-up through changes in the dermatological pattern, the appearance of nonspecific lesions, laboratory abnormalities, or systemic symptoms.

Nonspecific lesions deserve particular attention because they often correlate more strongly with systemic activity than some specific lesions. Nonscarring alopecia, oral or nasal ulcers, cutaneous vasculitis, livedo reticularis, Raynaud phenomenon, and photosensitivity may occur in patients with active SLE and are not always exclusive to lupus^{2,5}. However, their presence in patients with established or suspected lupus increases the need for systemic evaluation. Stull, Sprow, and Werth³ highlight that SLE activity indices, such as the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and SLEDAI-2K, incorporate cutaneous and

mucosal manifestations, including alopecia, ulcers, vasculitis, and rash, demonstrating that dermatological activity formally contributes to the measurement of systemic activity.³

In the study by Brahmanti, Wahono, Pratama, Rahman, Suhendra, Rizky, and Mukti⁸, alopecia was the most frequent nonspecific cutaneous manifestation, present in 46.3% of patients, followed by photosensitivity in 44.4%. Both were associated with significantly higher Mex-SLEDAI scores⁸. This finding is important because it broadens the analysis beyond classic lesions. In many clinical settings, manifestations such as alopecia and photosensitivity are considered less “dramatic” than nephritis or neuropsychiatric manifestations; however, within the overall disease spectrum, they may signal ongoing inflammatory activity.

Photosensitivity has a dual role: it is both a clinical manifestation and a triggering factor. Ultraviolet radiation induces keratinocyte damage, exposure of nuclear autoantigens, activation of plasmacytoid dendritic cells, and amplification of the type I interferon pathway.^{1,3,6,7} Thus, photosensitive patients not only develop cutaneous lesions after sun exposure but may also experience systemic exacerbations related to environmental stimulation. This mechanism makes photoprotection a therapeutic intervention with the potential to reduce cutaneous activity and possibly modulate the risk of exacerbations.

Oral and nasal ulcers, although not statistically associated with Mex-SLEDAI in the study by Brahmanti, Wahono, Pratama, Rahman, Suhendra, Rizky, and Mukti⁸, are relevant manifestations in classification criteria and may accompany systemic activity.^{2,5,8} The fact that a specific study did not demonstrate a statistical association does not eliminate their clinical relevance, since the presence of ulcers may vary according to the population, sample size, ongoing treatment, and timing of assessment. This is one of the main limitations of the literature on cutaneous lupus: many studies are cross-sectional, with small samples, and may capture only a single time point in a fluctuating disease.

Cutaneous vasculitis represents a particularly relevant manifestation because of its association with systemic activity. Unlike specific lesions such as discoid lupus, vasculitis is a nonspecific lesion, but its presence may indicate more intense systemic inflammation, vascular involvement, and a greater risk of association with other organs. In the study by Brahmanti, Wahono, Pratama, Rahman, Suhendra, Rizky, and Mukti⁸, vasculitis was strongly associated with the presence of SCLE, and cutaneous infections were associated with vasculitis and nephritis.⁸ Although cutaneous infection is not a classic manifestation of lupus activity, its association with higher Mex-SLEDAI scores suggests that patients with more active disease, greater immunosuppression, or impaired skin barrier function may be more vulnerable to infections.

The correlation between cutaneous manifestations and renal involvement should be interpreted with caution. Cutaneous lupus, in isolation, does not predict nephritis in all patients. However, certain findings, such as ACLE, nonspecific lesions, vasculitis, active serology, elevated anti-dsDNA, and hypocomplementemia, increase the need for renal screening.^{1,2,5} In the cited cross-sectional study, the presence of cutaneous infection was associated with nephritis, but this finding should not be interpreted as a direct relationship between infection and renal damage⁸; more likely, it represents an indirect marker of greater disease activity, immunosuppressive treatment, or systemic vulnerability.

Laboratory markers help qualify the correlation between the skin and systemic involvement. Anti-dsDNA and anti-Sm are more specific for SLE, although anti-Sm has lower sensitivity. Anti-dsDNA also has value in monitoring, since its levels tend to parallel disease activity, particularly nephritis, especially when associated with complement consumption.² In contrast, anti-Ro/SSA and anti-La/SSB are not specific for SLE, but are strongly associated with SCLE and photosensitivity.² Thus, laboratory interpretation should be guided by the cutaneous phenotype: malar rash and suspected systemic activity require assessment of anti-dsDNA, complement, complete blood count, urinalysis, and renal function; SCLE requires particular attention to anti-

Ro/SSA; localized discoid lupus may show lower serological positivity, but still requires baseline evaluation.

The pathophysiology described in the articles supports the idea that dermatological manifestations and systemic activity share common immunological pathways. Maz and Kahlenberg³ discuss the role of B lymphocytes, BAFF signaling, T cells, neutrophils, NETs, and plasmacytoid dendritic cells at the interface between cutaneous and systemic lupus. This perspective shifts the skin from a passive role to an active position within the immunological network of lupus. The cutaneous lesion may represent the visible site of systemic processes, but it may also contribute to maintaining the autoimmune response through the release of autoantigens, local cytokine production, and recruitment of inflammatory cells.

The type I interferon pathway is particularly relevant. Recent reviews indicate that interferon participates in immune activation in both cutaneous and systemic lupus, promoting dendritic cell maturation, B-cell activation, autoantibody production, and perpetuation of tissue inflammation.^{1,2,3,7} The central role of this pathway also explains the growing interest in targeted therapies such as anifrolumab and other molecules under investigation.⁹ Thus, the clinical findings regarding the correlation between cutaneous lesions and systemic activity are not merely observational; they reflect overlapping immunopathological mechanisms.

Another relevant point is the distinction between activity and damage. Cutaneous activity includes erythema, scaling, infiltration, recent lesions, nonscarring alopecia, and mucosal involvement. Damage includes scarring, atrophy, persistent dyspigmentation, and scarring alopecia.^{5,8} This distinction is fundamental to the present topic because not every visible lesion indicates current systemic activity. A patient with longstanding, scarred discoid lupus may have substantial dermatological damage but low systemic activity at that time. In contrast, a patient with a recent malar rash, photosensitivity, diffuse alopecia, and laboratory abnormalities may have little scarring but high systemic activity.

CLASI is the main specific instrument for measuring activity and damage in cutaneous lupus. It separates the activity score, CLASI-A, from the damage score, CLASI-D, allowing assessment of erythema, scaling, hypertrophy, mucosal involvement, alopecia, dyspigmentation, and scarring.^{2,5,8} This distinction is more sensitive for cutaneous lupus than systemic indices such as SLEDAI, which include some cutaneous manifestations but do not accurately capture the extent and severity of dermatological involvement across different subtypes.^{2,5}

The longitudinal study by Ker, Teske, Feng, Chong, and Werth⁹ makes an important contribution to understanding the evolution of cutaneous activity and damage. In a cohort of 83 patients with cutaneous lupus assessed using CLASI over time, patients with an initial CLASI-A greater than 9 had a higher probability of improvement in cutaneous activity, while patients with greater baseline damage also showed specific patterns of progression.⁹ The study showed that 72.73% of patients with an initial CLASI-A greater than 9 improved, compared with 14% of those with a CLASI-A less than or equal to 9.⁹ This finding may appear paradoxical, but it suggests that patients with greater initial inflammatory activity have a larger measurable margin for response to treatment.

The longitudinal analysis also demonstrates that cutaneous damage should not be used in isolation as a marker of systemic activity. Scarring, dyspigmentation, and scarring alopecia may persist even after inflammatory control.⁹ Therefore, in an article aimed at correlating dermatological manifestations with systemic activity, it is essential not to conflate accumulated damage with current activity. This distinction improves the methodological quality of the discussion and prevents erroneous conclusions, such as assuming that every patient with extensive cutaneous lesions necessarily has active systemic disease.

The literature also demonstrates a relevant impact of cutaneous manifestations on quality of life. Lesions in visible areas, such as the face and scalp, are associated with stigma, psychosocial impairment, anxiety,

depressive symptoms, and reduced self-esteem^{2,5,7}. Even in the absence of severe systemic activity, permanent cutaneous damage may cause substantial morbidity. This point broadens the discussion beyond biological correlation: dermatological manifestations have diagnostic, prognostic, therapeutic, and psychosocial value. Therefore, their assessment should not be considered secondary in rheumatological or clinical practice.

From a therapeutic perspective, the correlation between the skin and systemic activity supports an integrated approach. General measures, such as strict photoprotection, smoking cessation, review of medications associated with drug-induced SLE, and vitamin D replacement when indicated, form the basis of management^{2,7,9}. Localized lesions may be treated with topical corticosteroids or calcineurin inhibitors, whereas extensive, recurrent, or refractory disease often requires antimalarials, particularly hydroxychloroquine.^{2,7,9}

Therapeutic response may also provide information about disease activity. Patients with cutaneous manifestations associated with systemic activity may require immunosuppressive agents or biologic therapies according to the organ involved and disease severity. Recent reviews highlight emerging therapies such as belimumab, anifrolumab, lifilekimab, deucravacitinib, and enpatoran, reflecting the transition toward approaches guided by specific immunological pathways⁹. This perspective is relevant to the discussion because it reinforces that the skin may serve as a measurable endpoint in clinical trials and as a practical marker of therapeutic response.

Comparative analysis of the articles allows a clinical hierarchy of systemic risk to be proposed. ACLE, particularly recent and photoinduced malar rash, appears to be the manifestation most strongly associated with systemic activity. SLE occupies an intermediate position, with a strong serological association and photosensitivity, and may coexist with SLE, but often with a milder systemic course. Localized CLE shows a lower immediate systemic correlation, but a greater risk of permanent cutaneous damage. Nonspecific lesions—particularly vasculitis, alopecia, ulcers, Raynaud phenomenon, and photosensitivity—should be interpreted as potential markers of systemic activity, especially when they arise newly or are associated with laboratory abnormalities.¹⁻⁹

This hierarchy, however, should not be applied rigidly. The coexistence of different cutaneous subtypes in the same patient is possible, and temporal evolution may modify risk. Stull, Sprow, and Werth⁵ report that a proportion of patients may present with more than one type of cutaneous lupus, which makes simplistic classifications difficult. Thus, the prognostic value of dermatological lesions depends on the overall clinical context: subtype, extent, timing, inflammatory activity, damage, systemic symptoms, serology, complement levels, urinalysis, and renal function.

It is also important to consider the limitations of the analyzed studies. Part of the evidence derives from narrative reviews or cross-sectional studies, which are useful for clinical synthesis but do not establish causality. The study by Brahmani, Wahono, Pratama, Rahman, Suhendra, Rizky, and Mukti⁸, although relevant for quantifying the association between cutaneous lesions and Mex-SLEDAI, included a limited sample and a specific population, which may restrict the generalizability of the findings.⁸ The study by Ker, Teske, Feng, Chong, and Werth⁹, in turn, contributes a longitudinal analysis using CLASI, but primarily evaluates the cutaneous course and not necessarily systemic activity across all outcomes.⁹ Therefore, the discussion should acknowledge that the correlation between cutaneous and systemic involvement is consistent but heterogeneous, dependent on subtype, and still lacking larger prospective studies.

Despite these limitations, the findings are clinically coherent and convergent. Dermatological manifestations of lupus function as accessible markers of immunological activity, with particular value in longitudinal follow-up. The presence of malar rash, SLE, photosensitivity, alopecia, vasculitis, and ulcers should prompt

investigation of systemic activity through complete clinical examination, complete blood count, renal function, urinalysis, proteinuria assessment, complement levels, anti-dsDNA, and other autoantibodies according to the phenotype. In contrast, scarred discoid lesions should be evaluated with a focus on local activity, accumulated damage, risk of permanent alopecia, and the need to prevent sequelae.

In summary, the results indicate that there is a relevant correlation between dermatological manifestations and systemic activity in lupus, but this correlation is not uniform. The greatest systemic risk is concentrated in acute, subacute, and nonspecific manifestations associated with inflammatory activity, whereas localized chronic forms tend to reflect cutaneous damage more than systemic activity. This distinction is fundamental for guiding diagnosis, risk stratification, follow-up, and treatment. The skin should therefore be interpreted as a clinical interface between local inflammation and systemic disease and is indispensable for the early recognition of activity, prevention of damage, and individualization of care in lupus erythematosus.

CONCLUSION

The integrated analysis of this study allows us to conclude that the dermatological manifestations of lupus erythematosus function as a true “sentinel organ,” in which the morphology and chronology of lesions provide valuable information for predicting the systemic behavior of the disease. This correlation, however, is heterogeneous: while acute cutaneous lupus, such as malar rash, and nonspecific manifestations, such as vasculitis and alopecia, are strongly associated with systemic activity and higher Mex-SLEDAI scores, the chronic form tends to follow a course more limited to the skin, although with a greater potential for irreversible scarring damage.

The investigation demonstrated that laboratory and immunological markers—including the autoantibody profile (anti-dsDNA and anti-Ro/SSA) and complement consumption—help qualify this correlation, allowing clinicians to distinguish acute inflammatory activity from accumulated tissue damage. Thus, the early identification of these patterns and the use of validated instruments such as CLASI are essential for risk stratification and timely therapeutic management, while also helping to mitigate the disfiguring psychosocial impact of the lesions.

Finally, longitudinal follow-up is essential, since the patient’s clinical phenotype may shift between subtypes over time. The methodological limitations of the current literature highlight the need for further prospective studies to refine predictive factors for systemic progression. In summary, interdisciplinary integration between dermatology and rheumatology is established as a central pillar for anticipating internal organ involvement and optimizing the overall prognosis of patients with lupus.

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