Clinical and Dermatoscopic Features of Systemic Autoimmune Diseases: A Single-Center Prospective Study

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Abstract

Objectives: The aim of this study was to determine the diagnostic value of cutaneous manifestations in patients with various systemic diseases and to examine their association with systemic disease activity.

Methods: The study was conducted as a prospective single-center clinical observational analysis at the Dermatology and STD Clinic, Riga 1st Hospital, Riga, Latvia, including 112 patients who underwent clinical, dermatoscopic, morphological, and immunohistochemical evaluation of skin manifestations in the context of confirmed systemic disease.

Results: The study revealed distinct patterns of clinical, dermatoscopic, and histological skin involvement across the studied diseases. Among patients with systemic lupus erythematosus (SLE), the most common findings were macules (62%) and alopecia (51%), with 89% of rashes presenting a malar ("butterfly") configuration and photosensitivity. In systemic sclerosis, telangiectasias (59%) and firm papules (38%) were characteristic, while dermatoscopy detected crystalline structures in 41% of patients, indicating deep fibrotic remodelling of the dermis. Sarcoidosis presented with firm papules (51%) and translucent orange-yellow structureless areas on dermatoscopy in 51% of observations, corresponding to dermal granulomas. In rheumatoid arthritis, vasculitis was recorded in 48% of patients, accompanied by livedoid changes and follicular plugs (37%). Morphological analysis confirmed a predominance of T lymphocytes in lupus erythematosus (72%) and rheumatoid arthritis (78%), whereas macrophage infiltrates dominated in sarcoidosis and systemic sclerosis (up to 57%), showing differences in the predominant inflammatory cell populations.

Conclusions: Specific skin manifestations reflect systemic disease activity and can help dermatologists and rheumatologists guide diagnostic strategy, justify biopsy, and adjust treatment, though individual features overlapped across nosologies and were not fully specific on their own. Given the single-center design, these findings are preliminary and require confirmation in larger multicenter studies before routine clinical use; their prognostic value, in particular, requires longitudinal validation.

Keywords: Vasculitis; Fibrosis; Granuloma; T Lymphocytes; Macrophages; Hyperkeratosis; Telangiectasias.

Introduction

Cutaneous manifestations of systemic diseases may provide early clues to an underlying systemic disease. Skin lesions often appear before organ-specific symptoms and may accompany disease

onset or exacerbation. At the same time, the clinical importance of cutaneous symptoms is often underestimated due to their nonspecificity, variability in morphological presentations, and similarity to dermatoses of other aetiologies. In typical cases, skin changes mimic isolated dermatological conditions, complicating the establishment of a link with the systemic process and leading to misdiagnoses or delays in starting appropriate treatment. This problem is further aggravated by the lack of standardised diagnostic algorithms that would integrate dermatological symptoms into the overall diagnostic approach for systemic diseases.

The classification of cutaneous manifestations in systemic diseases remains challenging because of their considerable morphological variability. A structured classification of cutaneous manifestations, including classification by lesion type, localisation, and correlation with phases of the underlying disease activity, was proposed by Sampaio et al.[1] Particularly novel is the concept of patterns that may serve as markers of exacerbation or subclinical course. However, the classification presented by Leal et al.[2] reveals a significant gap in coverage of atypical clinical variants that do not fit established diagnostic categories. The presence of forms such as combined mucocutaneous lesions or isolated vasculitic elements emphasises the need to revise traditional assessment models. The complexity is further increased by skin manifestations in systemic lupus erythematosus (SLE), which are often underestimated in rheumatological practice. The publication by Stull et al.[3] analysed the limitations of current classification criteria, particularly their inability to encompass all clinical variants of skin involvement, potentially causing diagnostic delays and underestimation of disease severity.

The formation of dermatological symptoms in systemic diseases is driven not only by clinical factors but also by fundamental disturbances at the level of vascular endothelium, connective tissue matrix, and immune regulation. The study by Cutolo and Smith[4] analysed the role of microangiopathies as an underlying pathological mechanism shaping the clinical picture of telangiectasias, capillaritis, and ischaemic lesions in systemic sclerosis. The authors demonstrated a close association between microvascular abnormalities and the severity of cutaneous symptoms, supporting the role of angiopathic markers as prognostic indicators. From a fundamentally new perspective, the problem of local immune activity was examined in the work by Xu et al.,[5] which for the first time described the spatial organisation of fibroblast subpopulations responsible for cutaneous lesion patterns in autoimmune syndromes. The study's data indicate anatomical specificity in fibroblast activation across different skin areas, which has direct clinical relevance for predicting lesion types. The issue of chronicity of cutaneous inflammation was detailed in the study by Ryan et al.,[6] where resident memory T cells were identified as key effectors of persistent immune damage. It was demonstrated that local T cell populations form a stable proinflammatory microenvironment that sustains disease activity independently of systemic immune dynamics.

The epidemiological structure of skin manifestations in systemic pathology shows regional variability reflecting both the genetic heterogeneity of populations and differences in diagnostic resource availability. In a multicentre study by Ivanova et al.[7] conducted on a cohort of patients with systemic sclerosis in Latvia, a high frequency of pronounced cutaneous lesions at early disease stages was found. In particular, diffuse sclerotic changes predominated, indicating late diagnosis and insufficient dermatological stratification in early pathology detection. Data from Sokolovskis et al.[8] supplement this finding, demonstrating that chronic urticaria in the Latvian population often has an immunological basis and may be associated with latent systemic disturbances. The authors highlight the need for more detailed investigation of skin symptoms in such patients as potential predictors of systemic autoimmune processes. Regional data from the Arabian Peninsula point in a similar direction: in a hospital-based Omani cohort, Al Ismaili et al.[9] found that immune-mediated skin disorders – including discoid and SLE – were frequently accompanied by systemic comorbidity, illustrating how the local spectrum and recognition of autoimmune skin involvement differ between populations. The diagnostic value of instrumental methods was confirmed in the study by Liluashvili et al.,[10] where dermatoscopic signs characteristic of systemic connective tissue diseases were analysed. A novel finding was the establishment of correlations between visual patterns and the type of immune-mediated inflammation, enabling optimisation of primary diagnostic algorithms at the outpatient level.

Despite the growing body of research, several aspects remain insufficiently elucidated, notably the histopathological variability of cutaneous manifestations within the same nosological forms, their diagnostic value, and population specificity. Unlike most published studies, which examine a single disease or rely on one diagnostic method, the present work evaluates five systemic diseases within the same cohort using clinical, dermatoscopic, histological, and immunohistochemical assessment. This design makes it possible to compare disease-specific patterns of skin involvement under uniform conditions and to relate these findings to validated measures of disease activity. The inclusion of patients from Latvia also provides data for a population that remains underrepresented in the available literature. The aim of this study was to conduct a clinical evaluation of skin symptoms in patients with the five systemic diseases included in the study from the standpoint of their diagnostic significance and their association with systemic disease activity. The objectives of the study were: to identify clinically relevant types of skin lesions; to establish their association with systemic disease activity; and to assess the potential of dermatoscopy as an adjunct to clinical assessment.

Methods

This research was conducted as a prospective, single-centre observational study, which involved a comparative assessment of cutaneous manifestations and systemic activity without altering patient treatment or using experimental drugs. The duration was six months (November 2024 – April 2025 inclusive). The study took place at the Dermatology and STD Clinic, Riga 1st Hospital, Riga, Latvia, which has specialised expertise in managing patients with systemic connective tissue diseases. The medical setting provided a multidisciplinary approach involving specialists from relevant fields.

Patients aged 18 to 65 years who, during the recruitment period, presented to the clinic with dermatological symptoms accompanying a confirmed diagnosis of a systemic disease were included. The total sample size was 112 individuals. This study included all eligible patients who met the inclusion criteria during the predefined recruitment period. No formal sample size calculation based on effect size estimates was performed, and the sample size was determined by the number of eligible patients recruited during the predefined study period. The mean age of participants was 42.6±11.3 years. Women predominated – 82 individuals (73.2%), consistent with known epidemiological patterns of autoimmune pathology prevalence. Men numbered 30 (26.8%). The average disease duration at inclusion was 3.9±2.1 years. The cohort included patients with five systemic diseases. The largest group consisted of patients diagnosed with SLE – 37 individuals (33%). The second-largest group included patients with systemic sclerosis – 29 individuals (25.9%). Less represented were patients with sarcoidosis (16 individuals, 14.3%), Sjögren's syndrome (14 individuals, 12.5%), and rheumatoid arthritis with skin involvement (16 individuals, 14.3%). The selection of these five systemic diseases – SLE, systemic sclerosis, sarcoidosis, Sjögren's syndrome, and rheumatoid arthritis – was justified by their prevalence, diversity, and specificity of skin manifestations, as well as their importance for diagnosis and prognosis. These diseases may present diagnostic challenges and require a differentiated treatment approach to improve clinical outcomes and patient quality of life.

Patients were enrolled in the study based on preliminary screening and the presence of clearly defined inclusion criteria. Eligible participants had a verified diagnosis of one of the specified systemic diseases and clinically documented skin manifestations confirmed by a dermatologist. Before enrolment, all systemic diagnoses had been established by the treating specialists. Where applicable, medical records were reviewed against the 2019 EULAR/ACR classification criteria for SLE, the 2013 ACR/EULAR criteria for systemic sclerosis, the 2016 ACR/EULAR criteria for primary Sjögren's syndrome, and the 2010 ACR/EULAR criteria for rheumatoid arthritis. Sarcoidosis was diagnosed on the basis of compatible clinical and radiological findings, supported by histological confirmation where clinically indicated and exclusion of alternative granulomatous diseases. Because recruitment took place in a specialised dermatology clinic and required documented skin involvement, patients with more evident cutaneous manifestations may have been preferentially included. All dermatoscopic examinations were performed and interpreted by one dermatologist using predefined morphological criteria; interobserver agreement was therefore not assessed. A mandatory condition was the availability of signed written informed consent for participation. Exclusion criteria included patients with oncological, infectious, or toxic-allergic skin diseases potentially mimicking systemic dermatoses,

as well as those with decompensated somatic conditions, pregnant women, individuals with mental disorders preventing informed participation, or those who withdrew consent.

All study participants underwent a standard clinical dermatological examination, including assessment of morphological characteristics of skin lesions. The initial examination involved visual and palpatory identification of rash elements (macules, papules, purpura, telangiectasias, lichenification), their colour, borders, localization, symmetry, and distribution. Subjective symptoms (itching, pain, burning) and mucous membrane status were also evaluated. Lesion topography was recorded, classified as acral, periorificial, truncal, or generalized forms. Dermatoscopic examination was performed using a handheld Heine Delta 20T dermatoscope (Germany) with 10x magnification in polarized and non-polarized modes. Dermatoscopic examinations were performed using a standardized examination protocol, and all findings were recorded according to predefined assessment criteria. Assessed features included microvascular structures, hyperkeratosis, atrophy, telangiectasias, background erythema, as well as capillary loops, reticular vascular pattern, and crystalline structures diagnostically significant for systemic sclerosis, and SLE. Each dermatoscopic feature was recorded according to predefined morphological criteria based on its vascular architecture, colour, distribution, and surface characteristics. Each participant was assessed at a single time point; the study was therefore prospective in enrolment but cross-sectional in design, without longitudinal follow-up.

In 38 cases (33.9%), skin biopsy was performed based on clinical indications, according to routine clinical practice and the treating physician's judgment. Histopathological examination was therefore performed only in selected cases and was not intended as a mandatory diagnostic procedure for all study participants. Specimens were fixed in formalin, processed according to standard protocols, and stained with hematoxylin and eosin. Morphological evaluation included assessment of epidermal changes, infiltration, perivascular alterations, sclerosis, and vasculitis. Immunohistochemistry was applied in some cases with markers CD3 (T lymphocytes), CD20 (B lymphocytes), and CD68 (macrophages/histiocytes) to characterise the inflammatory infiltrate. Consultation with specialists from related fields (rheumatologist, pathologist, allergologist) was involved as needed, and their expert opinions were considered in the clinical assessment.

To accurately interpret the diagnostic significance of cutaneous manifestations, all patients underwent assessment of systemic disease activity using validated disease-specific activity indices. Systemic disease activity was assessed at the time of the dermatological examination using disease-specific validated indices. For SLE, the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) was employed, encompassing 24 clinical and laboratory parameters, including skin symptoms, nephritis, serositis, and anti-dsDNA antibody levels. The total score ranged from 0 to 105 points, based on weighted parameters. For systemic sclerosis, the Modified Rodnan Skin Score was used, involving palpation-based skin thickness assessment across 17 body areas (0-3 points each), with a maximum total score of 51. This score assesses the extent and severity of skin thickening. In sarcoidosis patients, activity was determined based on clinical and radiological data (Scadding staging), angiotensin-converting enzyme levels, skin and lymph node involvement, chest computed tomography findings, and pulmonary function tests. The EULAR Sjögren's Syndrome Disease Activity Index was applied for Sjögren's syndrome, covering 12 organ domains (including skin, vasculitis, arthritis, hematologic involvement), completed with rheumatologist involvement. For rheumatoid arthritis, the Disease Activity Score 28 (DAS28) index was used, considering the number of tender and swollen joints, Erythrocyte Sedimentation Rate or C-Reactive Protein levels, and patient global assessment on a visual analogue scale.

As this was a non-interventional observational study, no modifications were made to the patients' ongoing treatment during the study period. Therapeutic decisions remained under the responsibility of the treating physicians and were not influenced by the study protocol.

All collected data were processed statistically using IBM SPSS Statistics version 26.0 (USA). Initial analysis involved database formation and descriptive statistics: calculation of mean (M) and standard deviation for normally distributed metric variables, and median (Me) for variables with asymmetric distribution. Frequencies (n) and percentages (%) were determined for qualitative variables. Normality

was tested with the Shapiro-Wilk test. For normally distributed data, the Student's t-test (independent samples) was used; for non-normal data, the Mann-Whitney U test was applied. Spearman's correlation coefficient (ρ) was calculated to identify associations between cutaneous manifestations and systemic disease activity. No adjustment for multiple comparisons was applied. Therefore, statistically significant findings should be interpreted with appropriate caution. Confidence intervals for the correlation coefficients were not calculated, as the correlation analyses were exploratory and hypothesis-generating and, given the small disease-specific subgroups, were intended to describe the direction and strength of associations within this cohort rather than to provide precise interval estimates. Two-tailed tests were used, and a p-value <0.05 was considered statistically significant.

The study was conducted in accordance with international ethical standards and approved by the Local Ethics Committee of the Department of Dermatology and Venereology at Pauls Stradins Clinical University Hospital, Latvia. All patients provided written informed consent after receiving comprehensive information on the study's objectives, methods, and potential risks. Personal data processing complied with the European Commission's guidelines on ethics and data protection,[11] ensuring anonymity and restricted access.

Results

Clinical Forms and Topography of Cutaneous Manifestations

Skin manifestations in patients with systemic connective tissue diseases exhibited a broad clinical spectrum, reflecting both the pathogenetic features of the primary nosology and individual variants of immune response. Morphological types of skin lesions included macules, papules, telangiectasias, purpura, vasculitis, and alopecia. Their frequency and pattern varied significantly depending on diagnosis.

In patients with SLE, the most typical cutaneous manifestations included erythematous macules on the face forming the characteristic butterfly rash, frequently associated with photosensitivity. The lesions were symmetrically distributed and often accompanied by surface scaling. Alopecia was common, presenting as either patchy or diffuse hair loss with signs of follicular dystrophy and skin atrophy. Purpuric eruptions, appearing as petechiae or ecchymoses on the lower extremities, were associated with thrombocytopenia and elevated antiphospholipid antibody titres, indicating possible immune-complex-mediated vascular involvement.[12,13]

In patients with systemic sclerosis, the most common finding was telangiectasia, observed in 59% of cases. These appeared as small dilated vascular elements, most commonly located on the facial skin (cheeks, lips, chin), hands, chest, and the inner surfaces of the forearms. In 72% of cases, the telangiectasias exhibited a "tree-like" or "punctate" pattern. Firm papules or indurated plaques were recorded in 38% of patients. These lesions had a pearly or waxy appearance, distinct borders, were firm to the touch, and symmetrically localized on the fingers, dorsal surfaces of the hands, and forearms. Areas of sclerosis also showed zones of depigmentation or hyperpigmentation, accompanied by atrophy of sweat glands and decreased sensitivity. Most patients reported a sensation of skin tightness, and in some cases, difficulty opening the mouth (microstomia) due to sclerosis of the perioral region.

Cutaneous manifestations in Sjögren's syndrome were generally mild. Papules were mainly observed in areas prone to friction or dryness, whereas macules occasionally resembled nummular eczema. Xerosis, fissures, scaling, and pruritus were the predominant associated symptoms, often complicating the clinical differentiation from other inflammatory dermatoses.[14]

Cutaneous manifestations of sarcoidosis exhibited marked morphological variability. The most characteristic lesions were firm, painless reddish-brown papules, which frequently coalesced into plaques. Macular lesions appeared as hyperpigmented or hypopigmented patches without evident inflammatory signs. Some patients presented with subcutaneous nodules consistent with sarcoid

granulomas, while isolated cases demonstrated violet plaques on the nose or auricles consistent with lupus pernio.

Rheumatoid arthritis was associated primarily with dermatological signs of vascular involvement. Vasculitic lesions ranged from petechiae to deeper necrotic changes, predominantly affecting the lower legs. Purpura and livedoid or reticular vascular patterns were common manifestations, while some patients developed scarring alopecia with epidermal atrophy.[15] Cutaneous manifestations generally worsened during arthritis exacerbations and improved during clinical remission.

The topographical distribution of lesions reflected microvascular involvement patterns: acral zones were affected in 54% of cases, consistent with known pathophysiological mechanisms of microangiopathy in systemic sclerosis, SLE, and rheumatoid arthritis. Perioral lesions were characteristic mainly of systemic sclerosis (34%) and SLE (21%). Generalized forms predominated in sarcoidosis (62%). Symmetrical distribution of lesions was noted in 71% of patients, providing an additional differential diagnostic criterion for systemic processes. For systematization of the identified clinical dermatological phenotypes, a comparative analysis of the frequency of main types of skin lesions among patients with different nosological entities was conducted (Figure 1).

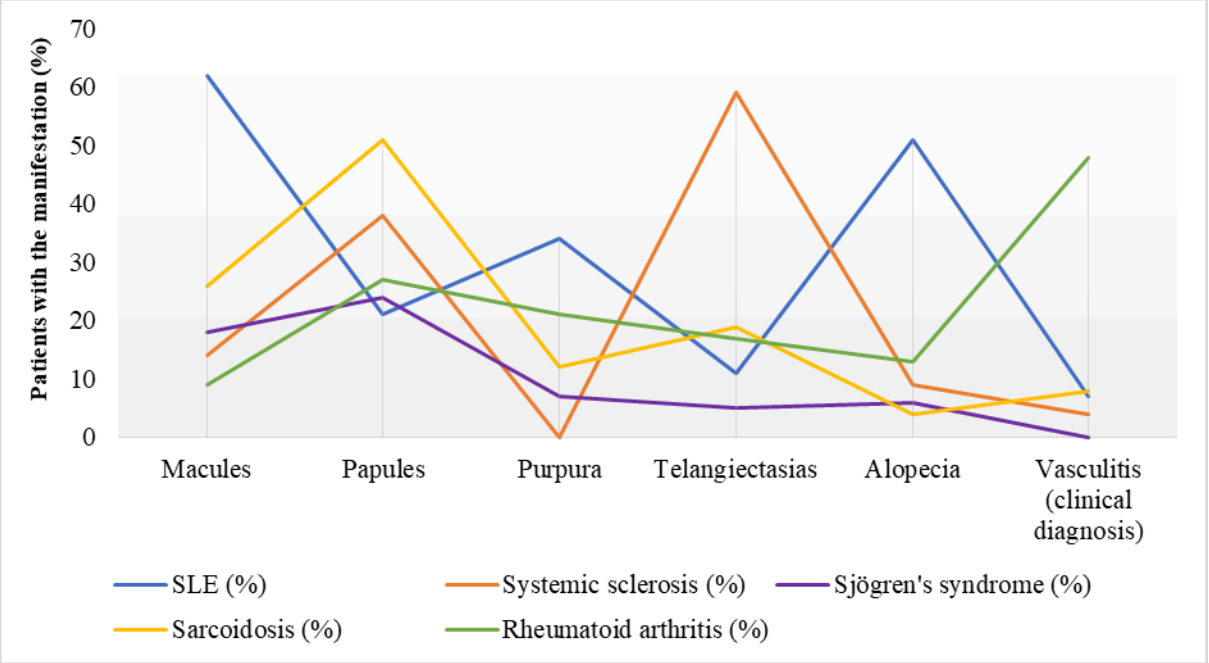

Figure 1: Prevalence of clinical forms of skin lesions in systemic diseases (%). Note: Percentages are calculated separately for each disease group.

Figure 1 illustrates differences in the frequency of the principal clinical manifestations across the evaluated diseases. The predominance of macules and alopecia in SLE was more frequently associated with higher disease activity in the studied cohort. Papulomacular lesions in sarcoidosis were compatible with granulomatous skin involvement. Together, these findings demonstrate recognizable patterns of skin involvement across the evaluated diseases, although overlap between conditions remains.

Dermatoscopic Features in Systemic Diseases

Dermatoscopy, as a non-invasive skin visualisation tool, allows for the detection of microscopic structural features that are inaccessible during routine clinical examination. Given the complexity of clinical phenotypes and the high risk of diagnostic errors at early stages, dermatoscopic analysis

provides additional objective information on the morphology of lesions and pathogenetic changes in the skin.

In patients with SLE, the most characteristic dermatoscopic features included telangiectasias in the form of dilated capillaries and capillary loops with central dilation, reflecting microcirculatory disturbances.[16] Diffuse background erythema correlated with clinically evident photosensitivity, while perifollicular erythema with mild scaling indicated follicular involvement, particularly on the scalp. In contrast, systemic sclerosis was characterised by reticular vascular structures and atypical capillary loops forming an irregular, fragmented network. Spiral-shaped telangiectatic vessels reflected pronounced vascular remodelling, whereas background hypopigmentation and crystalline structures with a shiny halo were typical of sclerotic lesions. Dermatoscopy in sarcoidosis, by comparison, demonstrated monomorphic straight vessels forming a homogeneous vascular pattern, accompanied by background hypopigmentation, hyperkeratotic follicular crusts, and orange-yellow structureless areas corresponding to granulomatous infiltration.[17] In rheumatoid arthritis, dermatoscopy was characterised by pinpoint haemorrhages and segmented vessels accompanied by diffuse background erythema reflecting chronic inflammation, while follicular plugs with surrounding white rings indicated prolonged follicular and epithelial damage. The summarised results of the analysed dermatological patterns are presented in Table 1.

Table 1: Dermatoscopic signs in systemic diseases.

Disease	Typical vascular patterns	Operational definition	Additional visual signs	Background pattern
SLE	Dilated capillary loops, telangiectasias	Dilated capillary loops: enlarged hairpin-shaped capillaries. Telangiectasias: permanently dilated superficial vessels visible on dermatoscopy.	Perifollicular erythema, hyperkeratosis, follicular plugs	Moderate erythematous background
Systemic sclerosis	Reticular vessels, spiraled capillaries	Reticular vessels: interconnected linear vessels forming a net-like pattern. Spiraled capillaries: coiled capillary loops with tortuous morphology.	Crystalline structures, atrophy, depigmentation	Pale hypopigmented background
Sarcoidosis	Straight monomorphic vessels, branching network	Straight monomorphic vessels: uniform linear vessels without marked tortuosity. Branching network: arborizing vascular structures.	Orange-yellow structureless areas, follicular crusts	Uniform pink-yellow structure
Rheumatoid arthritis	Pinpoint haemorrhages, segmented vessels	Pinpoint haemorrhages: small, well-defined red haemorrhagic dots. Segmented vessels: interrupted linear vessels composed of short vascular segments.	Livedoid patches, necrotic areas, follicular plugs	Intense erythematous background

Note: Crystalline structures were defined as bright, shiny white streaks visible under polarized dermatoscopy; orange-yellow structureless areas as translucent, ill-defined zones of orange to yellow-orange discoloration lacking identifiable dermatoscopic structures; follicular plugs as keratin-filled follicular openings; and background erythema as diffuse, homogeneous erythematous coloration surrounding the lesion.

The dermatoscopic patterns observed in this study differed between diseases and may provide additional information during clinical assessment. Some dermatoscopic findings, particularly crystalline structures in systemic sclerosis, were observed predominantly in one disease group. Papular or necrotic lesions in rheumatoid arthritis and sarcoidosis were accompanied by more monomorphic and symmetrical vascular patterns, whereas the infiltrative-granulomatous signs of sarcoidosis were clearly visualised as orange-yellow structureless areas. In summary, dermatoscopy provided additional morphological information that complemented clinical examination and may assist differential diagnosis when interpreted together with other clinical findings.

Correlation of Cutaneous Manifestations with Systemic Autoimmune Activity

The results demonstrate statistically significant correlations between the severity of dermatological symptoms and systemic autoimmune activity in several nosological groups, most clearly in SLE and systemic sclerosis. The strongest correlations were observed in patients with SLE, where the total SLEDAI-2K score showed a positive association with the intensity of background erythema and the number of telangiectasias ($\rho=0.58$, $p=0.003$), indicating a reliable relationship between cutaneous manifestations and systemic inflammatory activity. Hyperkeratotic perifollicular inclusions appeared to be associated with disease activity in the same direction.

In the systemic sclerosis group, the highest correlation was identified between the Modified Rodnan Skin Score and the extent of sclerotic papules and telangiectasias ($\rho=0.61$, $p=0.002$). The presence of crystalline structures on dermatoscopy, considered a marker of fibrotic-degenerative dermal changes, also reached statistical significance ($\rho=0.56$, $p=0.002$). These findings support the pathogenetic role of cutaneous fibrosis as a reflection of systemic connective tissue remodelling.

In sarcoidosis, moderate positive correlations were found between the Scadding stage of pulmonary involvement and the number of cutaneous telangiectasias ($\rho=0.45$), and between angiotensin-converting enzyme levels and the severity of orange-yellow structureless areas ($\rho=0.41$); given the small subgroup ($n=16$), neither association reached statistical significance (both $p>0.05$) and both should be regarded as exploratory trends consistent with the systemic nature of vascular and infiltrative changes. In rheumatoid arthritis, the DAS28 index was associated with livedoid changes, follicular plugs, and background erythema, with coefficients ranging from $\rho=0.43$ to $\rho=0.57$; only the stronger associations ($\rho\geq0.50$) reached statistical significance ($p<0.05$), whereas weaker associations represented non-significant trends. Overall, the observed correlations support an association between cutaneous manifestations and systemic disease activity in SLE and systemic sclerosis, with weaker, non-significant trends in the smaller sarcoidosis and rheumatoid arthritis subgroups; none of these associations should be interpreted as evidence of causality.

Morphological and Immunohistochemical Characteristics of Cutaneous Lesions

Morphological examination of skin biopsies was conducted in 38 patients with clinically significant cutaneous manifestations of systemic disease requiring histopathological verification. Histological assessment included the analysis of epidermal and dermal structure, vascular alterations, cellular infiltrate composition, and the presence of fibrosis and vasculitis. Immunohistochemistry was applied to detect major immune cell populations – T lymphocytes, B lymphocytes, and macrophages – enabling evaluation of the type of inflammatory response and underlying pathogenic mechanisms.

In patients with SLE, histological examination demonstrated vacuolisation of the basal layer with degenerative basement membrane changes and perivascular vasculitis with fibrinoid necrosis.[18] The inflammatory infiltrates were predominantly composed of T lymphocytes, consistent with a cell-mediated immune response. In contrast, systemic sclerosis was characterised by deep dermal sclerosis with fibrosis of the vessel walls and marked luminal narrowing. Classic vasculitis was uncommon, whereas immunohistochemical analysis showed a predominance of CD68+ macrophages, consistent with a fibrotic process. Similarly, sarcoidosis demonstrated non-caseating epithelioid granulomas, frequently lacking a peripheral lymphoid mantle, with inflammatory infiltrates dominated by CD68+ macrophages. By comparison, rheumatoid arthritis was characterised by

medium-vessel vasculitis with vascular wall necrosis, thrombosis, and neutrophilic infiltration, accompanied by acanthosis, atrophy, and parakeratosis.[19] Immunohistochemical analysis demonstrated a predominance of T lymphocytes, consistent with the autoimmune nature of the disease. A comparative analysis of the major inflammatory infiltrate cell types is presented in Figure 2

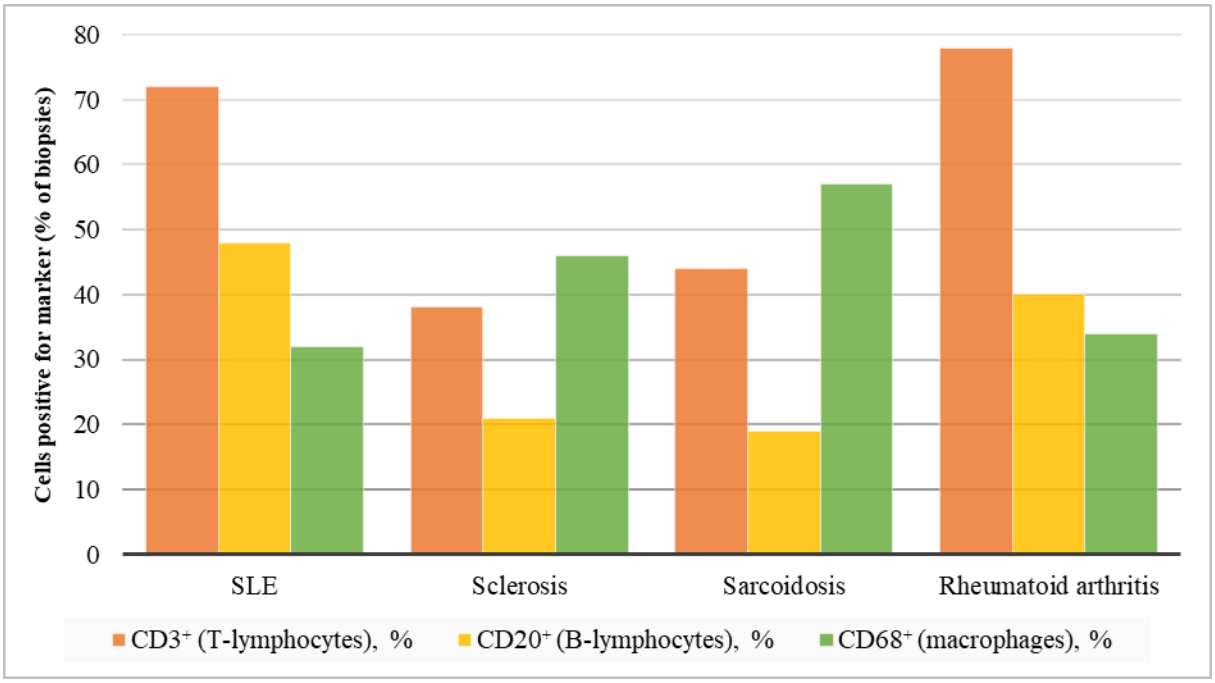

Figure 2: Frequency of inflammatory infiltrate cell populations (CD3, CD20, CD68) in the skin in systemic diseases. Note: Sjögren's syndrome not shown (biopsy not performed).

Analysis of the cellular composition of infiltrates revealed significant differences between disease groups. T lymphocytes predominated in SLE and rheumatoid arthritis, reflecting T-cell-mediated mechanisms of skin involvement. In contrast, macrophages dominated in systemic sclerosis and sarcoidosis, indicating a fibrotic or granulomatous nature of skin changes. B-lymphocyte activity was significant only in patients with SLE and rheumatoid arthritis, supporting the role of B-cell involvement as a component of pathogenesis. Differences in cellular infiltrates may contribute to understanding disease-specific inflammatory mechanisms and could complement histopathological assessment.[20] The combination of histological and immunohistochemical analysis provided additional information on disease-specific inflammatory patterns.

To facilitate comparison across disease groups and reduce reliance on the detailed narrative descriptions, the principal clinical, dermatoscopic, and morphological features, together with their associations with disease activity, are consolidated for each systemic disease in Table 2.

Table 2: Comparative summary of key clinical, dermatoscopic, and morphological/immunohistochemical features across systemic diseases.

Disease	Key clinical features (%)	Characteristic dermatoscopic features (%)	Dominant histology / immunohistochemistry	Correlation with disease activity
SLE	Malar (butterfly) macules 62% (facial 89%, photosensitive 73%); alopecia 51%; purpura 34%	Telangiectasias 78%; dilated capillary loops 71%; diffuse background erythema 69%; perifollicular	Basal-layer vacuolisation 63%; perivascular vasculitis 54%; T-cell predominant (CD3 72% > CD20 48% > CD68 32%)	SLEDAI-2K vs background erythema and telangiectasias : ρ=0.58 (p=0.003)

		hyperkeratotic deposits 53%		
Systemic sclerosis	Telangiectasias 59% (tree-like/punctate); firm papules / indurated plaques 38%; sclerosis, microstomia	Reticular vessels and atypical capillary loops 63%; telangiectasias 59%; hypopigmented background 52%; crystalline structures 41%	Deep dermal sclerosis 81%; vascular-wall fibrosis; classic vasculitis only 26%; macrophage predominant (CD68 46% > CD3 38% > CD20 21%)	mRSS vs sclerotic papules and telangiectasias: ρ=0.61 (p=0.002); crystalline structures ρ=0.56
Sarcoidosis	Firm reddish-brown papules 51% (coalescing plaques 38%); macules 26%; subcutaneous nodules	Monomorphic straight vessels 59%; orange-yellow structureless areas 51%; hypopigmentation 43%; follicular crusts 36%	Non-caseating epithelioid granulomas 74% (no lymphoid mantle 43%); macrophage predominant (CD68 57% > CD3 44% > CD20 19%)	Scadding stage vs telangiectasias: ρ=0.45 (NS); ACE vs orange-yellow structureless areas: ρ=0.41 (NS)
Sjögren's syndrome	Papules 24%; eczema-like macules 18%; xerosis, fissures, pruritus	Not assessed	Not assessed (biopsy not performed)	Not assessed
Rheumatoid arthritis	Cutaneous vasculitis 48% (petechiae to necrosis, lower limbs); purpura 21%; livedoid/reticular patterns	Background erythema 61%; segmented vessels 44%; follicular plugs 37%; pinpoint haemorrhages 33%	Medium-vessel vasculitis 61% (wall necrosis, thrombosis); T-cell predominant (CD3 78% > CD20 40% > CD68 34%)	DAS28 vs livedoid changes, follicular plugs and erythema: ρ=0.43-0.57 (significant for ρ≥0.50)

Note: mRSS – Modified Rodnan Skin Score; ACE – angiotensin-converting enzyme.

Table 2 highlights that, despite morphological overlap, each systemic disease displays a distinct combination of clinical, dermatoscopic, and immunohistochemical features. This consolidated comparison suggests that skin findings may complement differential diagnosis when interpreted together with laboratory and clinical data.

Discussion

The findings of this study allowed a detailed characterisation of the spectrum of cutaneous manifestations in systemic autoimmune diseases, which is of diagnostic value and links these manifestations to concurrent systemic disease activity. Analysis of the obtained data in the context of current literature made it possible to identify specific patterns of skin involvement correlated with various nosologies and their pathogenic mechanisms.

During the study, it was established that macules were the most common skin manifestation in patients with SLE, observed in 62% of cases, while alopecia occurred in 51%. The rash was predominantly localised on the face (89%), with 73% of patients presenting with photosensitive erythema. These findings correspond to the pathogenic role of cytokines in regulating inflammatory processes in the skin, as confirmed by Erazo-Martínez et al.,[21] who highlighted the key involvement of proinflammatory cytokines in the pathogenesis of skin lesions in SLE. Similarly, Gamal et al.[22] emphasised the frequent occurrence of vasculitis in this patient group, often associated with cutaneous manifestations such as erythema and telangiectasia. Abdel-Halim et al.[23] further

underscored the vascular alterations and immune-mediated reactions underlying the classical dermatological symptoms in autoimmune vasculitic processes, commonly observed in SLE patients.

In patients with systemic sclerosis, telangiectasia was identified in 59% of cases, indicating widespread microvascular involvement of the skin. Additionally, firm papules were detected in 38% of patients, serving as markers of fibrotic remodelling of the dermis and subcutaneous tissues. These clinical manifestations point to a progressive course of vascular dysfunction and fibroblast activation, contributing to collagen accumulation and fibrogenesis.[24,25] The predominant localisation of telangiectasia on the face and hands is consistent with data from Herrick et al.,[26] who identified telangiectasia as key markers of capillaropathy and vascular dysfunction at various disease stages. Jerjen et al.[27] emphasised the significance of these features as clinical indicators of fibrotic progression associated with microcirculatory impairment and fibroblast activation. Furthermore, Muruganandam et al.[28] highlighted the role of inflammatory biomarkers correlating with the extent of fibrotic involvement, reinforcing the close link between telangiectasia and papules and the pathogenesis of systemic sclerosis.

The study revealed that firm papules in sarcoidosis were present in 51% of patients, and in 38% of cases, these papules coalesced into plaques, indicating progressive granulomatous involvement of the skin affecting the deeper layers of the dermis. Monomorphic vessels were documented in 59% of patients, and along with orange-yellow structureless areas, these features were detected dermatoscopically, reflecting active inflammation. Such findings are characteristic of chronic cutaneous sarcoidosis and align with the underlying granulomatous inflammation.[29,30] Similar papular and plaque-like lesions associated with chronic progression and dermal granuloma formation were described by Lai et al.[31] The orange-yellow structureless areas and monomorphic vessels, considered characteristic dermatoscopic findings, were reported by Sève et al.[32] In addition, Nakamura et al.[33] noted the potential overlap between sarcoidosis and systemic sclerosis activity, underscoring the need for careful differential diagnosis.

The study found that vasculitis, in the form of haemorrhagic and livedoid lesions, was present in 48% of patients with rheumatoid arthritis, indicating the prevalence and clinical relevance of such lesions in the dermatological spectrum of rheumatoid arthritis. The lesions were predominantly located on the lower limbs, where vasculitic changes were often accompanied by marked inflammation and microcirculatory disturbances.[34] A similar frequency and character of vasculitic manifestations were described by Diaz et al.,[35] who highlighted the early onset of cutaneous vasculitis as clinical indicators of high systemic disease activity. Pathogenetically, vasculitis in rheumatoid arthritis is associated with immune complex formation and activation of cellular immune components, perpetuating inflammation and vascular wall damage.

Non-specific skin manifestations in patients with Sjögren's syndrome were observed in 24% of cases, including xerosis, papular rash, and fissures, reflecting impaired barrier function and reduced skin hydration. These changes are related to immune dysregulation and hyposecretion of exocrine glands, which contribute to skin dryness and increased sensitivity to environmental factors.[36-38] This clinical picture corresponds to the findings of Negrini et al.,[39] who described Sjögren's syndrome as a systemic autoimmune disorder with a broad range of extraglandular manifestations, including cutaneous involvement associated with B-cell activation, autoantibody production, and chronic inflammation. Additionally, a meta-analysis by Wirth et al.[40] confirmed that markers of systemic inflammation, particularly proinflammatory cytokines, may correlate with cutaneous and articular manifestations even when C-reactive protein levels are within the normal range, suggesting an indirect role of inflammatory activity in the development of skin symptoms. Thus, the non-specific skin changes identified in this study hold not only clinical but also pathogenetic relevance, making them an important component of the patient evaluation with Sjögren's syndrome.

The study revealed that dermatoscopic features in patients with SLE included telangiectasias in 78% of cases, dilated capillary loops in 71%, and perifollicular erythema in 53%, indicating pronounced vasculopathy and an immune-mediated inflammatory process in the skin. These dermatoscopic findings were associated with higher disease activity in our cohort and may provide additional information during follow-up. These findings are consistent with the data reported by

Chanprapaph et al.,[41] who emphasize the diagnostic value of trichoscopy and dermatoscopy in detecting specific signs of autoimmune dermatoses, particularly SLE. Furthermore, Pozharashka et al.[42] demonstrate that such changes correlate with clinical status and severity of cutaneous lesions. A systematic review by Guida et al.[43] also confirms the diagnostic significance of these dermatoscopic signs as part of the comprehensive evaluation of autoimmune skin disorders.

Several of the observed manifestations, including erythema, papules, telangiectasias, and vasculitic lesions, have broad differential diagnoses and may also occur in unrelated inflammatory dermatoses. Generalized pustular psoriasis, for example, may present with extensive inflammatory skin involvement and systemic complications, which underlines the need to interpret individual cutaneous findings within the wider clinical context rather than in isolation.[44,45] Dermatoscopy may assist this process by revealing vascular, follicular, and background patterns that are not evident on routine examination; its adjunctive role in the differential diagnosis and follow-up of connective tissue diseases has also been described by Liluashvili et al.[46]

The overlap observed across the disease groups confirms that none of these findings should be regarded as pathognomonic. Instead, combinations of clinical and dermatoscopic features may support a structured assessment alongside laboratory tests, organ evaluation, and histopathology where indicated. This is consistent with the observations of Sheikh et al.,[47] who reported that cutaneous phenotypes may provide early clues to underlying systemic disease, although they do not establish a specific diagnosis on their own.

Current diagnostic pathways for systemic autoimmune diseases remain centred on clinical assessment, serological testing, organ-specific investigations, and disease-specific classification criteria. Within this framework, dermatoscopy may help determine the next step in patient management: vascular changes may prompt closer assessment of disease activity or vascular complications, granulomatous patterns may guide selection of a representative lesion for biopsy, and suspicious findings in patients without an established systemic diagnosis may support rheumatological referral and targeted laboratory testing. In keeping with this, a recent report of cutaneous leukocytoclastic vasculitis illustrated how dermatoscopic features can help recognise vasculitic lesions and guide selection of the most appropriate biopsy site.[48,49]

Dermatoscopy can be performed during a routine consultation, provides an immediate result, does not require tissue sampling, and can be repeated during follow-up. These practical advantages make it a useful adjunct for triage, lesion selection, and documentation of change over time. The present study did not assess whether its use reduces biopsy rates, shortens the diagnostic pathway, or lowers healthcare costs; these outcomes require prospective clinical and economic evaluation.

This study has several limitations that should be considered when interpreting the findings. First, it was conducted at a single tertiary care centre with a relatively limited sample size, and no formal a priori sample size calculation based on effect size estimates was performed, as all eligible patients available during the predefined recruitment period were included; consequently, the statistical power to detect weaker associations may have been limited, and the generalizability of the findings should be interpreted with caution. Second, although patients were enrolled prospectively, each was assessed at a single time point, and this cross-sectional design precluded evaluation of longitudinal changes in dermatoscopic patterns during disease progression or in response to treatment; the potential influence of ongoing immunosuppressive or disease-modifying therapy was likewise not analysed separately. Accordingly, whether these activity-associated skin findings also carry prognostic value – predicting flares, progression, or treatment response – cannot be determined from the present data and should be addressed in prospective longitudinal cohorts. Third, histopathological confirmation was available only for selected patients according to clinical indications, and all dermatoscopic findings were assessed by a single observer, so interobserver reliability was not evaluated. Fourth, no adjustment for multiple comparisons was performed, and some statistically significant findings should therefore be interpreted with caution. Fifth, recruitment from a specialised dermatology clinic may have introduced referral and selection bias, with underrepresentation of patients with absent or subtle skin involvement. Finally, representative clinical, dermatoscopic, and histopathological images were not available for publication, as the study protocol did not include

standardized image acquisition or consent for image reproduction; the reported dermatoscopic and histological features were instead recorded descriptively using predefined morphological criteria. The resulting absence of illustrative images, together with the lack of complementary imaging techniques and molecular biomarkers, may limit the visual reproducibility and comprehensive diagnostic interpretation of the reported patterns. Future multicentre studies with larger cohorts, standardized photographic and histological documentation, and multimodal diagnostic approaches are warranted to validate and extend these findings.

Conclusion

Summarizing the results of the conducted study, several clinically significant conclusions can be drawn regarding the diagnostic value of cutaneous manifestations and their association with systemic disease activity. The data indicate that dermatologic phenotypes in systemic conditions differ markedly between disease groups and may provide supportive diagnostic information. For instance, the prevalence of butterfly-shaped erythema in SLE (89%) and telangiectasias in systemic sclerosis (59%) is consistent with their recognised clinical presentation. The acral distribution (54% of cases) and symmetry (71%) of lesions were frequently observed and are consistent with their systemic origin, while the morphological variability in sarcoidosis and rheumatoid arthritis reflects the heterogeneity of immune involvement. Thus, the topographic and morphological characterization of lesions may contribute to the clinical assessment of disease severity when interpreted together with other findings and may facilitate early diagnosis.

Dermatoscopy provided additional information beyond routine clinical examination. The high frequency of specific changes – such as dilated capillary loops in SLE (71%), crystalline structures in systemic sclerosis (41%), and monomorphic vessels in sarcoidosis (59%) – supports the use of dermatoscopy as an adjunctive diagnostic technique. The quantitative characteristics of identified patterns show that visualizing microvascular and follicular changes may reflect underlying pathological processes.

Statistically significant correlations were established (e.g., $\rho=0.58$ between telangiectasias and SLE activity, $p=0.003$; $\rho=0.61$ for papules in systemic sclerosis), supporting that skin findings reflect not only local changes but also systemic disease activity. This suggests that cutaneous findings may serve as candidate markers of disease activity; their value for predicting exacerbations or treatment response requires confirmation in longitudinal studies.

Morphological and cellular analysis of skin biopsies demonstrated that the nature of infiltrates is clearly disease-specific. For example, T lymphocytes predominated in SLE (72%), macrophages in systemic sclerosis (46%), and non-caseating epithelioid granulomas with macrophage predominance in sarcoidosis (57%). The frequency of verified vasculitis (54% in SLE, 61% in rheumatoid arthritis) indicates the impact of vascular involvement. These findings suggest that immunohistochemical assessment not only clarifies diagnosis but may contribute to the interpretation of inflammatory mechanisms and complement histopathological evaluation.

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