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Skin as a Window to Systemic Lupus Erythematosus

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Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by multisystem involvement and a highly variable clinical course that significantly affects patients' cosmetic appearance, functional capacity, and quality of life (1, 2). Cutaneous manifestations are among its most recognizable features and may precede, accompany, or occur independently of systemic disease (1, 3). Consequently, the skin represents more than a target organ; it may provide an important opportunity for the early recognition of underlying autoimmunity. However, the clinical potential of cutaneous findings has not been fully translated into structured pathways for systemic assessment, particularly in resource-constrained healthcare settings such as Pakistan.

In South Asian countries, including Pakistan, where published studies have documented substantial cutaneous and systemic involvement in lupus, strengthening the connection between dermatological recognition and rheumatological evaluation represents a meaningful clinical and research priority (2, 4, 5). A skin-centred approach could help improve early recognition, facilitate appropriate investigation, and support timely referral without treating cutaneous manifestations as definitive evidence of systemic disease.

1. Beyond Cutaneous Manifestations: Identifying Systemic Risk

Cutaneous lupus erythematosus encompasses a spectrum of manifestations, including acute, subacute, and chronic lesions, with discoid lupus, photosensitive eruptions, and lupus-associated alopecia among the clinically important presentations (3, 5). Some patients have disease predominantly confined to the skin, whereas others develop systemic manifestations involving the kidneys, joints, blood, nervous system, or cardiovascular system. Distinguishing these clinical trajectories is essential because the severity of cutaneous disease does not necessarily correspond to the extent of internal organ involvement.

Regional evidence reinforces the importance of this distinction. In a 2025 Pakistani study, Abowath and colleagues examined 135 patients with cutaneous lupus and reported systemic involvement, including renal involvement in 35.6% of the cohort (6). Similarly, a large Iranian cohort study by Akbarian et al. included 2,280 patients with SLE and reported cutaneous manifestations in 81.1% and renal involvement in 65.4% (7). These findings demonstrate the clinical relevance of skin disease in regional lupus populations, although differences in study design, patient selection, and diagnostic definitions prevent direct comparison of the reported proportions. The key question is therefore not simply whether skin manifestations occur frequently but whether specific clinical patterns can help identify patients who would benefit from earlier systemic evaluation (8). Addressing this question requires longitudinal research rather than relying exclusively on cross-sectional descriptions of disease prevalence.

2. The South Asian Perspective: An Unmet Research Opportunity

South Asian countries such as Pakistan provide valuable settings for collaborative lupus research. Their clinical populations and healthcare systems may differ in referral pathways, specialist availability, access to laboratory

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investigations, and continuity of care. These differences offer opportunities to investigate how clinical and healthcare-related factors influence recognition of systemic disease. Nevertheless, important uncertainties remain. It is not yet clear whether particular cutaneous phenotypes consistently predict subsequent systemic involvement in these populations, how frequently suspicious skin manifestations precede an SLE diagnosis, or how long patients wait between their initial dermatological presentation and definitive systemic assessment (9, 10). The contributions of socioeconomic circumstances, rural residence, health literacy, and access to multidisciplinary care also warrant systematic evaluation (9, 10).

A coordinated research programme could address these questions through prospective multicentre studies using standardized definitions of cutaneous manifestations and systemic outcomes. Investigators could record the intervals between the first skin manifestation, initial healthcare consultation, appropriate laboratory assessment, and rheumatology referral. Subsequent outcomes could include newly recognized SLE, renal involvement, diagnostic delay, and completion of specialist referrals. A collaborative study should recognize the distinct demographic and healthcare contexts of these populations rather than assume that all populations share a uniform regional disease phenotype. Such collaboration could identify common clinical priorities while revealing meaningful population-specific differences.

3. An Innovative Proposal: The Skin-to-Systemic Lupus Pathway

A Skin-to-Systemic Lupus (S2SL) pathway may serve as a conceptual framework for future clinical evaluation. Its central principle is to connect recognition of suspicious cutaneous findings with structured assessment for systemic disease and timely specialist referral. Under this proposed approach, dermatologists and primary care clinicians evaluating persistent photosensitive eruptions, characteristic discoid lesions, unexplained alopecia, mucosal ulceration, or other clinically suggestive manifestations would assess for accompanying systemic features. For practical implementation, the proposed S2SL pathway could follow a stepwise, risk-informed approach to avoid unnecessary investigations and referrals. Patients presenting with clinically suggestive cutaneous manifestations should initially undergo a focused clinical assessment, including a review of photosensitivity, oral or nasal ulcers, inflammatory joint symptoms, unexplained fatigue or fever, edema, and other features suggestive of systemic involvement. Relevant medical history and examination findings should also be documented. In patients with isolated cutaneous manifestations, no systemic symptoms, and no clinical indicators of internal organ involvement, immediate extensive autoimmune testing or routine rheumatology referral may not be necessary (11, 12). Dermatological assessment, appropriate evaluation of the skin disease, and clinical follow-up may be sufficient, with further investigation guided by the emergence of additional clinical features or persistent diagnostic suspicion (11, 12).

Laboratory investigations should be considered when cutaneous findings are accompanied by systemic symptoms, multiple suggestive clinical features, or other findings that raise suspicion of SLE. Initial investigations may include ANA testing, a complete blood count, serum creatinine or estimated glomerular filtration rate, and urinalysis with assessment for proteinuria. Where indicated, further investigations, including urine protein quantification, anti-double-stranded DNA antibodies, complement levels, and other relevant autoantibodies, may help guide subsequent evaluation (13). A positive ANA result should be interpreted in the context of clinical findings and should not independently trigger a diagnosis of SLE or automatic specialist referral. Referral to a rheumatologist would be appropriate when clinical findings and laboratory results collectively suggest possible systemic disease, particularly in patients with inflammatory joint manifestations, unexplained hematological abnormalities, persistent proteinuria, or other evidence of organ involvement. Patients with suspected renal involvement, significant proteinuria, active urinary sediment, or deteriorating renal function should receive prompt medical assessment and nephrology involvement where appropriate (13). Importantly, referral should not be delayed until all investigations are completed when significant organ involvement is suspected.

This tiered approach could help prioritize patients most likely to benefit from systemic evaluation while minimizing unnecessary investigations, financial burden, and specialist referrals among individuals with skin-limited disease. In resource-constrained healthcare settings, practical implementation could rely on focused clinical assessment, a limited initial investigation panel, clear referral criteria, and periodic reassessment. The proposed pathway should ultimately be evaluated prospectively to determine its diagnostic yield, safety, feasibility, and cost-effectiveness. Unlike routine clinical evaluation, which generally begins when SLE is already suspected on the basis of multisystem symptoms or established clinical criteria, the proposed S2SL pathway introduces a dermatology-initiated approach to identifying patients who may have unrecognized systemic

disease. Its principal innovation is not the introduction of additional diagnostic investigations but the systematic use of suspicious cutaneous manifestations as an opportunity to assess systemic risk, identify relevant clinical features, and initiate appropriate investigations or referral. Although previous dermatology-oriented approaches have emphasized screening for systemic lupus in patients presenting with cutaneous manifestations, the proposed S2SL pathway seeks to extend these concepts by integrating early clinical recognition, selective laboratory investigations, appropriate specialist referral, and evaluation of diagnostic delays, particularly in resource-constrained healthcare settings.

This approach may be particularly valuable in resource-constrained healthcare settings, where patients frequently encounter primary care clinicians or dermatologists before accessing rheumatological services. By incorporating a focused clinical assessment, selective laboratory investigations, and predefined referral considerations into routine dermatological consultations, the pathway could help reduce missed opportunities for early recognition without requiring extensive investigations in every patient. Furthermore, standardized documentation and shared referral criteria may improve communication among dermatology, primary care, and rheumatology services. Importantly, the S2SL pathway should complement, rather than replace, established diagnostic criteria and clinical judgment. Its potential advantages, including feasibility, cost-effectiveness, diagnostic yield, and reduction in referral delays, would need to be evaluated prospectively before routine implementation.

4. From Clinical Recognition to Collaborative Action

The success of this approach will depend on collaboration among dermatologists, rheumatologists, nephrologists, and primary care clinicians (14, 15). Shared referral criteria, standardized documentation, and accessible clinical guidance could help reduce fragmentation among specialties (14, 15). Research should also consider how cutaneous disease is recognized across different skin tones, particularly when erythema is less visually apparent. Patient-reported outcomes, scarring, pigmentary changes, photosensitivity, and psychosocial effects deserve inclusion alongside conventional measures of systemic disease. Standardized clinical photography and digital documentation could support longitudinal assessment, where appropriate, although their diagnostic value must be established before routine implementation. A regional registry incorporating harmonized clinical data could provide the foundation for future predictive models. Such models should be developed and externally validated before being used to guide clinical decisions. Their performance should be evaluated across different demographic groups and healthcare settings to avoid reinforcing existing inequalities.

The proposed S2SL pathway offers a conceptual framework for integrating dermatological recognition with targeted systemic assessment and appropriate specialist referral. Although this approach may facilitate earlier recognition of systemic disease, reduce diagnostic delays, and improve referral coordination, these benefits remain hypothetical and have not yet been established through clinical evaluation. Its implementation could provide an opportunity to investigate whether structured assessment of suspicious cutaneous manifestations improves the identification of previously unrecognized systemic involvement, particularly in resource-constrained healthcare settings. Future prospective multicentre studies should evaluate its feasibility, diagnostic yield, referral completion rates, time to definitive diagnosis, and cost-effectiveness. Importantly, these studies should also assess the potential for unnecessary investigations, false-positive findings, and avoidable specialist referrals. Until such evidence becomes available, the S2SL pathway should be regarded as a research-oriented proposal rather than an established clinical recommendation.

5. Conclusions

The skin offers a visible and potentially valuable opportunity to recognize SLE at an earlier stage. The priority should be to move beyond documenting cutaneous manifestations toward understanding their predictive value, measuring diagnostic pathways, and testing practical models of integrated care. The proposed Skin-to-Systemic Lupus pathway offers a research framework for connecting dermatological recognition with appropriate systemic assessment. Its potential to reduce diagnostic delays, improve referral coordination, and facilitate the identification of previously unrecognized systemic involvement remains to be established through prospective, multicentre validation. Such studies should also examine its feasibility, safety, and cost-effectiveness, particularly in resource-constrained healthcare settings. Collaborative regional research could help determine whether this approach can translate cutaneous findings into meaningful opportunities for earlier recognition and improved patient care.

Footnotes

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