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LICHEN SCLEROSUS – EPIDEMIOLOGY, TREATMENT, IMPACT ON QUALITY OF LIFE AND EMERGING THERAPEUTIC APPROACHES - A REVIEW

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ABSTRACT

Lichen sclerosus (LS) is a chronic, inflammatory skin disease with a complex, multifactorial etiology, encompassing immunological, genetic, hormonal, and environmental factors. The disease most commonly affects the anogenital region, leading to characteristic porcelain-white, atrophic plaques that can cause anatomical deformities, scarring, and impairments in sexual and urological function. LS symptoms are variable and include pruritus, pain, dyspareunia, urinary and bowel disturbances, as well as extragenital lesions in keratotic, bullous, or annular forms. The prevalence of LS differs between children and adults, and diagnostic delays can range from several months up to five years, increasing the risk of complications, including squamous cell carcinoma of the genital organs.

Diagnosis is primarily based on clinical examination, dermoscopy, and, in ambiguous cases, skin biopsy. Standard treatment includes topical glucocorticosteroids, with the possibility of maintenance therapy and adjunctive approaches such as calcineurin inhibitors, laser therapies, or systemic acitretin. Due to the chronic course of the disease and its impact on quality of life, patient care should be multidisciplinary, incorporating psychological support, sexual counseling and patient education.

The aim of this study is to provide a comprehensive overview of the clinical manifestations, diagnostic methods, therapeutic strategies, and consequences of LS for patient functioning. Emphasizing the importance of early diagnosis, monitoring of lesions, and patient education may contribute to improved treatment outcomes and quality of life for affected individuals.

KEYWORDS

Lichen Sclerosus, LS, Diagnosis, Treatment, Quality of Life, Anogenital Skin Lesions

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Introduction

Lichen sclerosus (LS) is a chronic, inflammatory dermatosis characterized by a complex, multifactorial etiology involving immunological mechanisms, genetic predispositions, hormonal disturbances, and environmental factors (5, 20, 24). The disease most commonly affects the anogenital region, causing porcelain-white, atrophic plaques that may lead to scarring, anatomical deformities, and impairments in sexual and urological function (9, 14, 17). In some cases, LS also occurs outside the genital organs, presenting as keratotic, bullous, annular lesions or following Blaschko lines, highlighting the phenotypic variability of the disease and complicating early diagnosis (2, 3, 8).

The impact of LS extends beyond direct dermatological symptoms- chronic pruritus, pain, dyspareunia, as well as aesthetic changes and anatomical deformities, impose a significant psychosocial burden on patients, including reduced quality of life, social isolation, and sexual dysfunction (4, 10). Diagnostic delays, which may result from nonspecific symptoms, misdiagnoses, or barriers to specialized care, increase the risk of complications such as the development of squamous cell carcinoma of the genital organs, chronic scarring lesions, and difficulties in treatment (5).

Despite numerous studies on LS pathogenesis and treatment, there remains a need for a systematic compilation and analysis of data regarding clinical manifestations, disease course, diagnostic methods, and therapeutic strategies. Such an approach would improve understanding of the disease's impact on patient functioning and optimize clinical care (4, 5). The aim of this review is to present the current state of knowledge on lichen sclerosus, including the characterization of clinical manifestations according to sex, diagnostic methods, available therapeutic options, and the disease's consequences for patient quality of life. The review also aims to emphasize the importance of early diagnosis, patient education, and multidisciplinary care in the effective management of the disease.

Methodology

This study was based on a systematic review of the scientific literature on lichen sclerosus (LS), encompassing topics related to epidemiology, clinical manifestations, disease course, diagnosis, treatment, and the impact of the disease on patient quality of life. The analysis included articles published in English and Polish between 2003 and 2025 (1-24), including systematic reviews, prospective and retrospective studies, review articles, and clinical guidelines. Source selection was based on titles, abstracts, and full texts, with inclusion criteria encompassing publications describing LS symptoms, clinical course, diagnosis, and treatment in both adults and children (3, 5, 14, 22), containing quantitative or qualitative data enabling the assessment of symptom prevalence, complications, and treatment outcomes (4, 5).

Articles focusing on other dermatoses without reference to LS, as well as publications describing single case reports without generalizable results, were excluded. Literature searches were conducted in PubMed, Google Scholar, and ScienceDirect using keywords such as “lichen sclerosus,” “lichen sclerosus et atrophicus,” “vulvar lichen sclerosus,” “genital lichen sclerosus,” “extragenital lichen sclerosus,” “diagnosis,” “treatment,” “dermatoscopy,” “confocal microscopy,” and “quality of life”. References from selected review and systematic review articles were also utilized (4, 5, 9).

Data were extracted across five main domains: epidemiology and risk factors; clinical manifestations and disease course, including sex-based differences; clinical diagnosis and supportive tools (including dermoscopy, confocal microscopy, and biopsy); pharmacological and non-pharmacological treatment; and complications, as well as the impact of LS on patient functioning, quality of life, and mental health (1, 5, 6, 7, 10, 16, 21). Each source was evaluated for methodological rigor, relevance to the topic, and reported limitations to ensure a high-quality review.

Epidemiology and Genetics

Lichen sclerosus (LS) primarily affects adult women, with a male-to-female incidence ratio of 1:10, and only 0.3% of cases occurring in children (9, 24). In women, two incidence peaks are observed-before menarche and during menopause-suggesting a possible role of hormonal factors in the pathogenesis of the disease (12, 20). Familial occurrence of LS, estimated at approximately 12% of cases, indicates a significant genetic component, and reports of twin cases as well as familial cases in siblings and parents further support the hypothesis of hereditary predispositions (20, 24).

Genetic studies have demonstrated clinical associations between LS and specific HLA types, including HLA-DQ7 and HLA-DR17, suggesting that genetically determined immunological mechanisms predispose individuals to the chronic inflammatory state characteristic of the disease (5, 20). Moreover, LS is more frequently diagnosed in patients with Turner syndrome (approximately 17.3%), highlighting the role of chromosomal aberrations in increasing susceptibility to disease development (14).

Co-occurrence of LS with autoimmune disorders, such as hypothyroidism, vitiligo, psoriasis, rheumatoid arthritis, systemic sclerosis, and type 1 diabetes, observed in 20-30% of patients, further supports an immunological basis for the disease (8, 11, 20). The role of the ECM1 protein, a regulator of immune responses and tolerance, has also been demonstrated in LS pathogenesis through autoimmune mechanisms targeting ECM1, as well as effects on regulatory T cells, Th2 cells, and B cell activation (20).

Overall, epidemiological and genetic data indicate that LS is a disease with a complex etiology, involving environmental, immunological, and multigenic genetic predisposition, as well as autoimmune mechanisms.

Etiology

Lichen sclerosus (LS) may have an autoimmune basis, with immune response dysregulation-including a predominance of Th1 lymphocytes-playing a key role in disease pathogenesis. Elevated levels of Th1-associated cytokines, dense T-cell infiltrates, increased BIC/miR-155 expression, and the presence of autoantibodies against extracellular matrix protein 1 (ECM1) and BP180 antigen have been observed (11, 20). However, other studies indicate that the presence of autoantibodies only minimally correlates with disease activity and treatment efficacy (19).

Increased expression of microRNA-155 (miR-155) promotes Th1 differentiation, disrupts regulatory T cell function, inhibits tumor suppressor genes FOXO3 and CDKN1, induces autoimmunity, and enhances collagen synthesis, explaining the chronic nature of the disease and the development of typical skin lesions (12).

Interferon amplifies the Th1 response and increases the number of Th1 cells. Additionally, LS is associated with elevated levels of other proinflammatory cytokines, such as IL-1 α , IL-7, IL-15, and TNF- α , while levels of anti-inflammatory cytokines, including IL-10, are reduced. The imbalance between pro- and anti-inflammatory cytokines contributes to the persistence of inflammation and tissue degradation (5).

Oxidative stress, characterized by lipid and DNA peroxidation and mutations in the TP53 gene, creates an environment conducive to autoimmunity and carcinogenesis. Mutations in the TP53 tumor suppressor gene may contribute to a slightly increased risk of vulvar cancer (squamous cell carcinoma) (5, 11). Chronic ulcerations, non-healing lesions with mixed pigmentation, and tissue structural heterogeneity require biopsy, as the estimated risk of LS-related malignancy ranges from 3-8% (9, 22). Differentiated vulvar intraepithelial neoplasia (dVIN) is a type of VIN arising from chronic vulvar inflammation and represents a premalignant lesion associated with lichen sclerosus (20).

Clinical guidelines recommend regular follow-up every few months and patient education regarding self-monitoring of skin lesions. Due to the increased risk of malignancy, patients with genital LS should undergo long-term, regular surveillance, whereas extragenital LS is not associated with an increased risk of malignant transformation (11).

Currently, LS is not considered to have an infectious etiology. Although *Borrelia burgdorferi*, HCV, and HPV were previously suggested as potential contributors, recent studies indicate that infectious agents do not play a significant role. The lack of clear evidence for pathogen involvement has led to the rejection of earlier infectious hypotheses, redirecting attention to genetic and immunological mechanisms (5).

Historically, hypoestrogenism was suggested as a risk factor due to the higher prevalence of vulvar LS in postmenopausal women and prepubertal girls. However, the proposed protective effect of estrogens has not been confirmed (5, 17). Trauma to the genital area, including friction, scratching, or surgical procedures, may act as triggering factors for LS, a phenomenon known as the Köbner response (9, 11).

Epidemiological data suggest that the true prevalence of LS is likely underestimated, ranging from approximately 0.1-0.3% of the population, with a clear predominance of women over men (20, 24). The disease can occur at any age but shows a bimodal peak: in prepubertal girls and postmenopausal women, as well as in middle-aged men (20, 24). Estrogen deficiency may affect the structural integrity of the skin, exacerbating LS symptoms in these age groups (5). Chronic LS can lead to scarring, urinary dysfunction, sexual problems, and an increased risk of malignancy, particularly poorly differentiated squamous cell carcinoma (20).

Clinical Manifestations and Disease Course

Approximately 9% of lichen sclerosus (LS) cases are asymptomatic, with the disease most commonly affecting the anogenital region. In women, lesions involve the labia majora and minora as well as the clitoris, whereas in men, they affect the foreskin, glans penis, and coronal sulcus (3, 9, 23). Perianal involvement is observed in approximately 30% of patients and may cause painful defecation, anal fissures, or bleeding, sometimes requiring gastroenterological consultation (9, 19).

Early lesions appear as white, polygonal papules, often accompanied by petechiae or telangiectatic changes. Over time, these evolve into atrophic, porcelain-white plaques, which may coalesce into larger areas and lead to scarring. Lesions frequently form a figure-eight pattern around the vulva and anus, highlighting the chronic, progressive nature of the disease (9, 17). Chronic inflammation may also cause hypo- or hyperpigmentation, impacting patients' psychological comfort and delaying medical consultation.

The main symptoms of LS include pruritus, pain, dyspareunia, dysuria, and anatomical changes leading to scarring, such as narrowing of the vaginal introitus, atrophy of the labia minora, or clitoral resorption in women, and phimosis or foreskin resorption in men (13). Ulcerations, erosions, constipation, and urinary or fecal incontinence may also occur. Lesions are recurrent, with periods of improvement alternating with flares, which complicates treatment adherence and management (19).

LS can have a profound impact on quality of life, particularly in the context of the genital region, disrupting intimate relationships and daily functioning (10, 22). In women, the most frequently reported symptoms were pigmentary changes (21%), pruritus (18%), and loss of normal vulvar and introitus architecture (14%), whereas in men, the dominant symptoms were loss of normal genital architecture, including adhesions, scarring, fissures, and phimosis (34%), as well as pigmentary changes and genitourinary symptoms (each 15%) (4).

Defecation-related symptoms, such as constipation, painful defecation, or rectal bleeding, were rare in women (1%), and asymptomatic LS was slightly more common in men (2%) (4). Diagnostic delays are common and lead to poorer outcomes, including deformities of the skin and mucosa, genitourinary problems,

and increased cancer risk. In children, diagnostic delays average over 20 months in girls and 2 months in boys, while in adults, delays can extend up to 5 years. LS is also frequently misdiagnosed-children may be suspected of abuse, whereas adults may be misdiagnosed with herpes, allergies, or candidiasis (4).

Extragenital lesions occur less frequently, affecting the axillae, neck, wrists, thighs, upper back, and shoulders, typically asymptotically. These lesions may present in various forms-keratotic, bullous, annular, or following Blaschko lines-underscoring the phenotypic variability of LS and the need for thorough clinical assessment (3, 8, 9).

Diagnosis

The diagnosis of lichen sclerosus (LS) in adults and children is primarily based on clinical examination and a thorough medical history. This includes the assessment of characteristic skin lesions-porcelain-white, atrophic plaques-primarily located in the anogenital region, although extragenital lesions may also occur (1, 2, 5). Early-stage disease is difficult to recognize because symptoms can be subtle, atypical, or asymptomatic (7, 8).

Photographic documentation is recommended to monitor treatment efficacy and disease progression. The clinical scoring system in vulvar lichen sclerosus (VLS) is a validated tool that facilitates diagnosis, evaluation of associated symptoms, and assessment of treatment response. Screening for autoimmune diseases should also be performed, especially in patients with symptoms suggestive of thyroid disorders, type 1 diabetes, rheumatoid arthritis, or systemic sclerosis (16).

Dermoscopy is a useful non-invasive tool for supporting LS diagnosis and optimizing the site of potential biopsy. In VLS, the most common dermoscopic feature is structureless white or white-yellow areas on a white atrophic background, reflecting dermal sclerosis and hyalinization. Another characteristic feature is reduced vascular density compared with normal vulvar skin. Early-stage VLS reveals irregular linear vessels in over 97% of cases and dotted vessels in nearly 45%, whereas in later stages, most vessels disappear due to dermal fibrosis (16). Other dermoscopic observations include scattered gray-blue dots, comedo-like opening, and scales. In extragenital LS (eLS), the most common findings are whitish structureless areas, comedo-like openings, telangiectasias, and dotted vessels in early stages. White structures resembling pupae, rosettes, or four-dot signs may be present but are not specific (16).

In ambiguous cases or when complications are suspected, a skin biopsy is performed from active sclerotic areas or erosions that do not improve with therapy. Early, ulcerated, or erythematous lesions are not suitable for biopsy, as they often display nonspecific histological features. Prior treatment with topical corticosteroids may also obscure characteristic histopathological changes (16).

Reflectance confocal microscopy (RCM) is another non-invasive in vivo imaging method. In male genital LS (MGLS), nearly half of patients show prominent fiber-like structures indicative of hyaline sclerosis, and an atypical honeycomb pattern may suggest the presence of penile intraepithelial neoplasia (16).

Differential diagnosis should include lichen planus, vitiligo, systemic lupus erythematosus, systemic sclerosis, psoriasis, graft-versus-host disease, cutaneous candidiasis, cicatricial pemphigoid, genital intraepithelial neoplasia, and squamous cell carcinoma (2, 9). Early diagnosis, including in asymptomatic or extragenital cases, is crucial for preventing complications, while patient education supports timely treatment initiation and long-term monitoring (1, 9, 16, 19, 23).

Treatment

The aim of lichen sclerosus (LS) therapy is to alleviate symptoms, prevent scarring, limit anatomical deformities, and reduce the risk of malignant transformation (3).

First-line treatment consists of potent topical glucocorticosteroids, most commonly clobetasol propionate (0.05%) or mometasone furoate ointments, applied once or twice daily for approximately three months. Ointments are preferred over creams due to their superior efficacy (20, 21). Topical therapy reduces symptoms and improves skin appearance, with remission achieved in approximately 60-70% of patients (5, 20, 21). Due to frequent relapses, maintenance therapy and regular skin monitoring are necessary; premature discontinuation of treatment (“steroid phobia”) increases the risk of recurrence and complications, highlighting the importance of patient education (5, 22).

Second-line treatment includes calcineurin inhibitors (tacrolimus, pimecrolimus), used in patients with an incomplete response to glucocorticosteroids. These agents alleviate symptoms, although their clinical efficacy may be slightly lower than that of steroids (7, 11, 24). An important component of supportive therapy is daily skincare using emollients and avoidance of irritants (3, 14). Additional beneficial approaches may

include herbal baths, silk clothing (Dermasilk), and local PDRN injections combined with glucocorticosteroids, which improve patients' comfort and quality of life (24).

Surgical treatment is reserved for complications or for cases limited to the foreskin in men. Circumcision is an effective method, while preputioplasty supported by subcutaneous steroid injections can also be beneficial but is associated with a higher recurrence risk compared with topical therapy. Corticosteroid ointments are also used in surgical management as adjunctive therapy or in cases of recurrence (14, 15).

Adjunctive and advanced therapies include:

- Laser therapies (CO₂, Nd:YAG, Er:YAG) and photodynamic therapy (PDT), which improve symptoms, skin elasticity, lesion color, and patient quality of life, with the highest efficacy observed for CO₂ laser (24).

- Systemic treatment (e.g., acitretin) in refractory or advanced cases, reducing pruritus, atrophy, and hyperkeratosis (24).

In summary, topical glucocorticosteroids remain the gold standard for LS treatment, while adjunctive therapies such as calcineurin inhibitors, PDRN, laser therapy, or acitretin may be used in combination regimens, particularly in patients with recurrent or treatment-resistant disease, with individualized therapeutic planning (3, 4, 7, 11, 14, 15, 17-22, 24).

Impact on Quality of Life and Psychosocial Aspects

Lichen sclerosus significantly reduces patients' quality of life. Symptoms such as pruritus, burning, pain, and discomfort during sexual intercourse limit daily functioning, negatively affecting comfort at work, during physical activity, and sleep, as well as intimate life (11, 22). Changes in the appearance of the genital area, including skin discoloration, induration, and scarring, may lead to decreased libido, feelings of shame, and anxiety related to sexual activity. Sexual dysfunction often results in difficulties in partner relationships, a sense of isolation, and symptoms of depression and anxiety (11, 22).

Studies have shown that more than 50% of women with LS report a significant deterioration in sexual quality of life, and persistent symptoms such as pruritus and pain increase psychological stress. The literature indicates that multidisciplinary support-including sexual health specialists, psychologists, and urogynecological physiotherapists-is an essential component of comprehensive care. Patient education, early diagnosis, and appropriate topical or systemic treatment reduce anxiety related to the potential development of malignancy, alleviate disease symptoms, and improve overall well-being and sexual functioning (1, 11, 22). Long-term psychological support should be an integral part of care for patients with LS.

Regular consultations with mental health professionals, structured psychosocial interventions-including cognitive behavioral therapy and counseling-may improve coping strategies, enhance treatment adherence, and strengthen patients' sense of agency. A holistic approach, combining pharmacological and surgical treatment, daily skin care, and psychosocial support, enables patients to maintain proper functioning and a satisfying sexual life regardless of age.

Predispositions and Risk Factors: A Clinical Perspective

Lichen sclerosus (LS) is a disease with a complex etiology involving the interplay of genetic, immunological, hormonal and environmental factors. Epidemiological analysis confirms a clear sex predisposition-women are affected approximately ten times more frequently than men, while the disease is rare in children, occurring in less than 0.3% of cases (9, 24). The observed bimodal peak of incidence in women, before menarche and during menopause, suggests a potential hormonal role in modulating skin and immune responses (12, 20, 24).

Although earlier theories proposed a protective role of estrogens, empirical data have not provided conclusive evidence to support this hypothesis (5, 17, 24).

Familial cases of LS and observations in twins clearly indicate a significant genetic basis of the disease (1, 20). Immunogenetic studies have demonstrated associations between LS and specific HLA types, including HLA-DQ7 and HLA-DR17, suggesting a predisposition to dysregulated immune responses and chronic inflammation (5, 18, 24). Additionally, the higher prevalence of LS in patients with Turner syndrome (~17.3%) highlights the role of chromosomal aberrations and developmental abnormalities in increasing disease susceptibility (14).

The coexistence of LS with autoimmune diseases, such as hypothyroidism, vitiligo, psoriasis, and type 1 diabetes, is common and affects 20-30% of patients (8, 11, 20). This association suggests that LS is not an isolated dermatological condition but rather part of a broader autoimmune spectrum, in which dysregulation

of the immune response leads to chronic tissue changes. A key role in this process is played by the ECM1 protein, which regulates immune responses and tolerance; autoimmune mechanisms directed against ECM1, along with dysfunction of regulatory T cells and Th2 cells, further promote chronic inflammation and scarring (20, 24).

Overall, epidemiological and genetic data confirm that LS is a multifactorial disease in which the interaction between genetic predisposition, immune dysregulation, and modulating hormonal and environmental factors determines both disease risk and clinical course (5, 9, 20).

Immunological Mechanisms as the Basis of LS Chronicity

The pathogenesis of lichen sclerosus (LS) is strongly associated with dysregulation of the immune response, as demonstrated by numerous immunohistochemical and molecular studies. LS is characterized by a predominance of Th1 lymphocytes, elevated levels of proinflammatory cytokines, and local lymphocytic infiltrates, which together lead to chronic inflammation and tissue damage (5, 11, 24). Th1 cytokines such as IFN- γ , IL-1 α , IL-7, IL-15, and TNF- α are significantly elevated, whereas anti-inflammatory cytokines, including IL-10, show reduced expression (5). The imbalance between pro- and anti-inflammatory factors promotes the persistence of chronic inflammation and degradation of skin structure, ultimately resulting in atrophy, scarring, and the characteristic porcelain-white lesions (12, 19). One of the key regulators in LS is microRNA-155 (miR-155), whose overexpression promotes Th1 differentiation and disrupts the function of regulatory T cells (12, 24). The literature emphasizes that miR-155 inhibits the expression of tumor suppressor genes such as FOXO3 and CDKN1, which may explain both the chronic nature of the disease and the increased risk of malignant transformation within vulvar lesions (5, 12). Increased miR-155 expression is also associated with enhanced collagen synthesis, accounting for the characteristic sclerosis and scarring observed in LS (5, 12).

Autoimmunity directed against extracellular matrix protein 1 (ECM1) represents another important component of LS pathogenesis. Autoantibodies against ECM1 disrupt normal skin function, influence B-cell and T-cell activation, and exacerbate chronic inflammation (20, 24). These mechanisms explain the coexistence of LS with other autoimmune diseases as well as the tendency for recurrence despite topical therapy (8, 11).

Oxidative stress, associated with lipid and DNA peroxidation and mutations in the TP53 gene, creates an environment conducive to both autoimmunity and potential carcinogenesis (5, 11). TP53 mutations may represent one of the intermediate factors increasing the risk of squamous cell carcinoma within genital lesions, estimated at 3-8% of LS cases (9, 22). Chronic exposure to oxidative stress further enhances scarring processes and atrophic skin changes, which, in combination with immunological and genetic disturbances, forms a self-perpetuating pathogenic mechanism (5, 12).

Despite extensive evidence supporting autoimmune and molecular mechanisms, some aspects remain controversial. For example, the presence of autoantibodies against ECM1 or BP180 does not always correlate with disease severity or treatment response (19). Variability in study results may stem from population heterogeneity, small sample sizes, or differences in diagnostic methodologies. At the same time, the lack of clear infectious evidence has led to the rejection of earlier hypotheses regarding the involvement of *Borrelia burgdorferi*, HCV, or HPV in LS etiology, further emphasizing the importance of immunological and genetic factors (5).

Understanding these mechanisms has important clinical implications—it highlights the need for therapies targeting not only clinical symptoms but also modulation of the immune response and reduction of chronic inflammation. Currently, these strategies are primarily implemented through topical glucocorticosteroids and calcineurin inhibitors; however, a growing body of research suggests the potential for targeted molecular therapies in the future (7, 11, 24).

Disease Course and the Importance of Patient Monitoring

The chronic nature of lichen sclerosis (LS) is one of the main factors complicating both diagnosis and treatment. Although approximately 9% of cases are asymptomatic, most patients report persistent pruritus, pain, dyspareunia, and difficulties with urination and defecation, significantly reducing quality of life (9, 13, 23). Anogenital lesions are progressive and lead to scarring and anatomical deformities, such as narrowing of the vaginal introitus, atrophy of the labia minora, clitoral resorption in women, and phimosis or foreskin resorption in men (9, 13). These complications largely result from chronic inflammation supported by previously described immunological mechanisms, including Th1 predominance, miR-155 overexpression, and autoantibodies against ECM1 (5, 12, 20).

A significant clinical aspect of LS is the increased risk of malignancy, particularly vulvar squamous cell carcinoma (SCC) and differentiated vulvar intraepithelial neoplasia (dVIN), which may arise as a consequence of chronic inflammation and atrophic changes (9, 20, 22). Malignant transformation is estimated to occur in 3-8% of patients, with the highest risk observed in long-standing, untreated lesions or chronic ulcerations (9, 22). These observations highlight the necessity of regular patient follow-up, including biopsy of suspicious or non-healing lesions, in accordance with current guidelines (6, 7, 11, 12, 13, 20).

The diagnosis of LS requires a combination of clinical assessment, dermoscopy, and, in uncertain cases, histopathological biopsy. Dermoscopy enables identification of subtle skin structures, such as white patches, follicular keratotic plugs, and scaling, which aid in differentiating LS from other dermatoses, including lichen planus, vitiligo, and localized scleroderma (1, 6, 9, 16). Histological examination typically reveals a lymphocytic infiltrate at the dermoepidermal junction, epidermal atrophy, hyperkeratosis, and dermal fibrosis (15).

The relationship between immunopathological mechanisms and clinical manifestations is also crucial in the context of disease recurrence. Relapses of LS are common, particularly following premature discontinuation of topical glucocorticosteroids ("steroid phobia") or inadequate skin care, leading to persistence of chronic inflammation and progressive scarring (5, 20, 22). Molecular mechanisms, including miR-155 overexpression and Th1 activation, may explain the recurrent nature of lesions and the need for long-term monitoring and maintenance therapy (12, 24).

The importance of LS diagnosis and monitoring extends beyond topical treatment alone. Early diagnosis and patient education enable prompt initiation of therapy and reduce the risk of complications, including malignant and psychosocial consequences (1, 9, 16, 19, 23). A holistic approach that incorporates immunological, genetic, and psychosocial factors is becoming essential in clinical practice. Patients who understand the chronic nature of the disease and the role of immune dysregulation demonstrate better adherence to therapy and actively participate in monitoring skin changes, thereby reducing the risk of complications (10, 11, 22).

The treatment of LS remains challenging due to its chronic, relapsing course and the phenotypic variability of skin lesions. High-potency topical glucocorticosteroids, such as clobetasol propionate 0.05% or mometasone furoate, remain the gold standard and are typically applied once or twice daily for approximately three months (5, 20, 21). This therapy not only alleviates symptoms such as pruritus and pain but also slows scarring, reduces skin atrophy, and lowers the risk of malignant transformation (5, 20).

However, even the most effective topical therapy requires long-term monitoring and maintenance treatment, as discontinuation increases the risk of relapse (5, 22). In clinical practice, "steroid phobia"- patients' fear of using glucocorticosteroids-is frequently observed and may lead to premature discontinuation and disease worsening (22). In such cases, patient education becomes essential; understanding that chronic inflammation and Th1 activation sustain disease activity improves treatment acceptance and adherence (12, 24).

In patients with an incomplete response to corticosteroids, calcineurin inhibitors such as tacrolimus and pimecrolimus serve as alternative options. Although slightly less effective clinically, they exert immunomodulatory effects by reducing T-cell activity and enhancing control of chronic inflammation (7, 11, 24). Supportive measures, including emollients, proper hygiene, and avoidance of irritants, are also important, as they reduce mechanical skin damage and the Köbner phenomenon, thereby minimizing inflammatory activation (3, 14).

In recent years, increasing interest has been directed toward adjunctive therapies that improve patient comfort and quality of life. These include PDRN injections, laser therapies (CO₂, Nd:YAG, Er:YAG), and photodynamic therapy (PDT) (24). Among these, CO₂ laser therapy demonstrates the highest efficacy in improving clinical symptoms and skin elasticity, while also potentially reducing scarring risk. In severe, refractory, or recurrent cases, systemic treatment with acitretin may also be considered, as it reduces hyperkeratosis and skin atrophy (21, 24).

However, therapeutic approaches should not be limited to pharmacological treatment alone. The psychosocial aspects of LS play a crucial role in patient quality of life. Chronic pruritus, pain, dyspareunia, and aesthetic changes lead to feelings of shame, social isolation, and decreased libido, as confirmed by studies in which more than 50% of patients reported deterioration in sexual quality of life (10, 11, 22). Persistent symptoms also increase psychosocial stress and the risk of depression and anxiety (11, 22).

A holistic approach involves multidisciplinary collaboration, including psychological support, consultations with sexual health specialists, and urogynecological physiotherapy. Such interventions, combined with appropriately tailored pharmacological treatment, enable patients to better cope with the chronic nature of the disease, reduce emotional burden, and improve treatment adherence (1, 10, 11).

The literature also emphasizes the importance of patient education and early diagnosis in preventing complications and improving treatment outcomes. Knowledge of the disease, understanding of immunological and genetic mechanisms, and awareness of the risk of malignant transformation allow patients to actively participate in monitoring lesions and responding promptly to relapses (1, 9, 16, 19, 23).

In summary, the management of LS requires an integrative and individualized approach that combines topical and adjunctive therapies, regular clinical monitoring, patient education, and psychosocial support. The coexistence of immunological, genetic, and psychosocial factors in disease pathogenesis underscores the need to consider LS not only as a dermatological condition but as a chronic disorder with both medical and psychosocial dimensions (5, 9, 10, 11, 20, 22).

Conclusions

Lichen sclerosis (LS) remains a chronic disease with a complex and multifactorial etiology involving genetic, immunological, and environmental determinants. Epidemiological data indicate a clear female predominance, with two incidence peaks-before puberty and after menopause- suggesting a potential role of hormonal factors and estrogen deficiency in disease pathogenesis (9, 12, 20, 24). Familial occurrence and associations with specific HLA types, such as HLA-DQ7 and HLA-DR17, further highlight the importance of genetic components in predisposing to chronic inflammation (5, 18, 20).

From both etiological and clinical perspectives, LS can be considered an autoimmune disease characterized by Th1-dominated mechanisms, miR-155 overexpression, and the presence of autoantibodies, including those directed against ECM1 (5, 12, 20, 24). Dysregulation of the balance between pro- and anti-inflammatory cytokines, chronic oxidative stress, and autoimmune mechanisms contribute to the development of characteristic skin lesions, recurrent disease course, and the risk of scarring and malignant complications, including squamous cell carcinoma and differentiated vulvar intraepithelial neoplasia (dVIN) (5, 9, 20, 22).

Diagnosis of LS requires a combination of careful clinical evaluation, dermoscopy, and, in uncertain cases, histopathological biopsy. Early recognition is essential not only to limit physical complications but also to improve patient quality of life, including psychosocial and sexual aspects (1, 6, 9, 10, 16).

Treatment remains primarily topical, based on high-potency glucocorticosteroids, supported by adjunctive therapies such as calcineurin inhibitors, PDRN, laser therapy, photodynamic therapy (PDT), or systemic acitretin in refractory cases (5, 7, 11, 21, 24). A holistic approach combining pharmacological treatment with patient education, proper skin care, and psychosocial support enables long-term disease control, reduces recurrence rates, and improves quality of life (1, 9, 10, 11, 22).

Despite advances in understanding LS pathogenesis and treatment strategies, many aspects remain unclear, including the precise role of hormonal factors, the specificity of genetic predispositions, and the mechanisms leading to malignant transformation (5, 12, 24). Further interdisciplinary research is needed to deepen knowledge of molecular and immunological mechanisms and to facilitate the development of targeted, personalized therapies that may improve outcomes and reduce recurrence and complications.

In summary, LS requires an integrated clinical approach that addresses both medical and psychological dimensions. Patient awareness, early diagnosis, regular monitoring, and individualized treatment remain key elements of effective management, minimizing complications and improving quality of life for affected individuals (1, 5, 9, 10, 11, 20, 22).

Lichen sclerosis is a chronic inflammatory skin disease with a complex, multifactorial etiology involving immunological, genetic, hormonal, and environmental factors. Available evidence clearly demonstrates strong associations between LS and autoimmune diseases, specific HLA types, and dysregulation of Th1-mediated immune responses, confirming the multidimensional nature of its pathogenesis.

LS is associated with a significant clinical burden. Characteristic skin changes, including porcelain-white plaques and atrophic scarring, lead to anatomical deformities and functional impairments such as dyspareunia, urinary and bowel dysfunction, and reduced tissue mobility within the genital area. In anogenital LS, there is a clinically significant increased risk of squamous cell carcinoma and differentiated vulvar intraepithelial neoplasia (dVIN), necessitating early diagnosis, regular follow-up, and biopsy of chronic or non-healing lesions. Delayed diagnosis-often due to nonspecific symptoms, psychosocial barriers, and sex-related differences in presentation-remains a major clinical challenge and underscores the importance of patient education and long-term surveillance (16).

LS diagnostics should be multidimensional. In addition to clinical examination, dermoscopy plays a crucial role by revealing characteristic white or yellow-white structureless areas, telangiectasias, and reduced vascular density in vulvar skin, facilitating appropriate biopsy site selection. Reflectance confocal microscopy

represents another non-invasive tool, enabling visualization of structures corresponding to dermal sclerosis and early histopathological changes, particularly in male genital LS (16). Biopsy remains indicated in unclear cases, non-healing lesions, or when malignancy is suspected.

Therapy for LS should be individualized and multifaceted. High-potency topical glucocorticosteroids remain the gold standard, effectively controlling symptoms in most patients. However, the relapsing nature of the disease necessitates maintenance therapy, appropriate skin care, avoidance of irritants, and regular clinical monitoring. In refractory or advanced cases, adjunctive treatments-including calcineurin inhibitors, laser therapies, photodynamic therapy, and systemic acitretin-may improve patient outcomes and limit disease progression.

The impact of LS extends beyond dermatological consequences. Chronic pruritus, pain, dyspareunia, and aesthetic changes contribute to reduced quality of life, feelings of shame, social isolation, sexual dysfunction, and frequent symptoms of depression and anxiety. Therefore, patient care should be multidisciplinary, incorporating psychological support, sexual counseling, and, when necessary, urogynecological physiotherapy. A holistic approach promotes better adherence to treatment, active patient participation in disease monitoring, and improved overall well-being.

Future research should focus on advancing understanding of the molecular and immunological mechanisms underlying LS, identifying reliable prognostic biomarkers, and developing novel targeted therapeutic strategies that enable personalized treatment and reduce the risk of recurrence and malignant complications. In clinical practice, increasing awareness among primary care physicians and patients regarding early LS symptoms, promoting prevention of complications, and emphasizing the importance of regular monitoring are equally essential.

In conclusion, LS remains a chronic disease with a multifaceted pathogenesis that requires a comprehensive approach-integrating pharmacological treatment, psychosocial support, clinical diagnostics supported by dermoscopy and confocal microscopy, patient education, and monitoring of malignancy risk. Only through the integration of these elements can effective disease management, improved quality of life, and reduction of long-term health consequences be achieved (16).

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