11. Tuberculosis surveillance and monitoring in Europe 2024. 2022 data. Copenhagen, WHO Regional Office for Europe. 182 p. https://doi.org/10.2900/44801.
12. Verkuijl S, Bastard M, Brands A, Viney K, Masini T, Mavhunga F, et al. Global reporting on TB in children and adolescents: how far have we come and what remains to be done? IJTLD Open. 2024 Jan 1;1(1):3-6. doi: 10.5588/ijtldopen.23.0529.
13. WHO, Roadmap towards ending TB in children and adolescents. Geneva, World Health Organization, 2018. License: CC BY-NC-SA 3.0 IGO.
14. World Health Organization. Global tuberculosis report 2022. World Health Organization, 2022. Available: https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022 Accessed October 1, 2024.
15. World Health Organization. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva, Switzerland 2018.

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DIAGNOSTIC CRITERIA FOR LOCALIZED SCLERODERMA

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Localized scleroderma remains a complex diagnostic challenge due to diverse clinical manifestations and a lack of prognostic markers. A study of 113 individuals analyzed demographic, clinical, and laboratory parameters, including vascular endothelial growth factor levels, to assess vascular dysfunction. The disease demonstrates significant gender and age specificity, with onset peaks among young men and older women. Most lesions are plaque forms at the induration stage, indicating late clinical detection. Vascular endothelial growth factor has been shown to be an objective severity indicator, correlating directly with the extent of fibrosis. Based on these results, a novel multilevel prognostic model was developed that integrates risk factors, morphology, and angiogenesis markers. This model holds significant value for global dermatology, enabling the timely identification of high-risk patients, predicting the clinical course, and preventing irreversible tissue changes through early, personalized treatment.

Keywords: localized scleroderma, vascular endothelial growth factor, prognostic model, disease severity, endothelial dysfunction, risk factors.

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ДІАГНОСТИЧНІ КРИТЕРІЇ ЛОКАЛІЗОВАНОЇ СКЛЕРОДЕРМІЇ

Локалізована склеродермія залишається складною діагностичною проблемою через різноманітність клінічних проявів і відсутність чітких прогностичних маркерів. У дослідженні за участю ста тринадцяти осіб було проаналізовано демографічні, клінічні та лабораторні показники, зокрема рівень фактора росту ендотелію судин для оцінки дисфункції судин. Встановлено, що хвороба має суттєву гендерну та вікову специфіку, з піками дебюту серед молодих чоловіків і жінок старшого віку. Більшість уражень представлена бляшковою формою на стадії ущільнення, що вказує на пізнє клінічне виявлення. Доведено, що фактор росту ендотелію судин є об'єктивним індикатором тяжкості патології, адже його концентрація прямо корелює з площею фіброзу. Спираючись на ці результати, розроблено новітню багаторівневу прогностичну модель, яка об'єднує фактори ризику, морфологію та показники ангіогенезу. Ця модель має вагоме значення для світової дерматології, оскільки дозволяє своєчасно виокремлювати пацієнтів із високим рівнем ризику, прогнозувати клінічний перебіг та запобігати незворотним змінам тканин шляхом ранньої персоналізації лікування.

Ключові слова: локалізована склеродермія, фактор росту ендотелію, прогностична модель, тяжкість захворювання, ендотеліальна дисфункція, фактори ризику.

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Scleroderma is a complex autoimmune disease that affects the skin, joints, blood vessels, and internal organs [15]. At a certain stage, the body begins to actively synthesize antibodies directed against the vascular endothelium (the inner lining of blood vessels). Subsequent inflammation of the endothelial lining of small capillaries leads to thrombosis. Consequently, the tissues supplied by these vessels

undergo ischemia and necrosis, which are replaced by inelastic, nonfunctional fibrous scar tissue [6]. Given its pronounced cutaneous manifestations, the disease derives its name from the dermis: the affected area becomes coarse, indurated, inelastic, and sclerotic. When this fibrotic process is confined to a specific, local area of the body, localized scleroderma develops [12].

Localized scleroderma (LS) remains one of the most significant challenges in modern medicine [12]. Discussions persist within the scientific community regarding the clinical and pathogenetic unity between localized and systemic forms of the disease [8]. Many researchers view LS as a cutaneous variant of systemic sclerosis, emphasizing its systemic nature despite the predominantly local character of the lesions [12].

The development of this pathology is driven by a multifactorial mechanism involving immune system dysfunction, microcirculatory disorders, and metabolic imbalances in connective tissue components [15]. Significant roles are attributed to autoimmune and infectious factors, which trigger a distorted allergic response, vasospasm, and accelerated collagen synthesis [5]. Key markers of immunological pathogenesis include elevated autoantibody titers and disproportionate blood protein fractions [14].

To date, there is no universally accepted classification of LS. The most widely utilized are the Mayo Clinic classification and the Padua criteria (2004), but different their interpretations are widely used in recent years [2, 11]. Five primary forms are identified: plaque, linear, generalized, deep, and mixed. The clinical course usually progresses through three stages: erythema/edema, sclerosis (induration), and atrophy [2]. Disabling forms, such as pansclerotic scleroderma and progressive facial hemiatrophy (Parry–Romberg syndrome), pose a particular clinical problem, leading to profound tissue deformities.

The diagnosis of LS is primarily based on the clinical presentation, as specific laboratory tests have not yet been developed [10]. Although parameters such as hypereosinophilia, antinuclear antibody levels, and rheumatoid factor may correlate with disease activity, they are not universal. Insufficient understanding of the relationship between clinical forms and endothelial function necessitates refinement of diagnostic criteria [10]. Consequently, the multifaceted nature of clinical manifestations and the absence of clear prognostic markers make improving the diagnostic principles of localized scleroderma a highly relevant issue in modern dermatology.

The purpose of the study was to substantiate and formulate specific diagnostic criteria for localized scleroderma based on clinical and instrumental data, and to develop a prognostic model for risk assessment across various patient populations.

Materials and methods. The study was conducted through an international academic collaboration involving National Pirogov Memorial Medical University (Vinnytsya), Jordanian Royal Medical Services (Amman), Ministry of Health of Jordan (Amman), Ministry of Health (State of Kuwait), RAK Medical & Health Sciences University (UAE), and Dr. Sulaiman Al-Habib Medical Group (KSA). Investigators from Jordan, KSA, Kuwait, and the UAE played a pivotal role in the execution of this study; their instrumental contributions encompassed advanced data analysis, the translation and clinical classification of laboratory investigations, conceptual synthesis, and the final refinement of the manuscript.

Informed consent was obtained from the adult participants and the children's parents or legal guardians, alongside assent from the children themselves.

The study cohort consisted of 113 individuals, divided into a main group (n=78; 69 %) and a control group (n=35; 31 %). All 78 patients in the main group diagnosed with LS received inpatient treatment at the Vinnytsia Regional Clinical Dermatovenereological Center between 2022 and 2025. The control group comprised healthy volunteers without LS examined at the same center. The inclusion criteria for the control group were: age- and sex-matching with the primary group, absence of skin pathologies, and no history of systemic diseases

Gender analysis showed a predominance of females (n=73; 64.6 %) compared to males (n=40; 35.4 %). The mean age of patients in the primary group was 43.2±7.28 years (range: 10–81 years), while the mean age in the control group was 39.5±8.10 years (range: 27–55 years).

The diagnosis of LS was established based on a combination of clinical presentation and histopathological verification.Study inclusion criteria: presence of LS in patients with an established diagnosis (typical erythema, edema, and induration); absence of signs of systemic involvement; eligibility for participation according to the study protocol; and voluntary, written informed consent. This consent explicitly permits clinical examination, the collection and analysis of diagnostic test results, and the utilization of patient medical data for research purposes, fully compliant with ethical requirements and the principles of the Declaration of Helsinki (2022).

Exclusion criteria included malignancy or mental disorders; pregnancy or lactation; decompensated chronic diseases or acute infectious pathologies; history of CNS trauma; recent use of drugs affecting the clinical course of LS; substance abuse; and withdrawal of consent. Diagnosis verification followed the ICD-10 (2019). Clinical management strictly adhered to the S1 guidelines of the European Dermatology Forum (EDF, 2017). Therapeutic strategies were individualized based on disease severity and activity according to established European evidence-based recommendationsfor localized scleroderma.

Comprehensive clinical evaluation determined the LS subtype and disease activity.Evaluation of internal organs was conducted only when systemic involvement was suspected.To evaluate disease activity and patient quality of life, specific dermatological indices and validated questionnaires were utilized. Disease activity was assessed using a 100-mm Visual Analog Scale (Physician Global

Assessment of Activity, PhysGA-A) to evaluate consensus-based clinical and laboratory signs, defining activity by the severity of reversible cutaneous and extracutaneous manifestations. Patient quality of life was measured using the Dermatology Life Quality Index (DLQI), a validated 10-item questionnaire (score range 0–30) that assesses the impact of the skin condition over the preceding week.

Venous blood samples were collected in the morning after fasting. Routine tests included CBC (Abacus 3CT, DIATRON MI PLC, Hungary), and biochemical screening(Diagon Ltd, Hungary). Specialized immunological profiling measured antinuclear antibodies (ANA) and immunoglobulin classes (IgA, IgM, IgG). Endothelial dysfunction and inflammatory activity were assessed using ELISA for vascular endothelial growth factor (VEGF).Laboratory analyses were performed using automated and semi-automated systems (Eppendorf BioSpectrometer spectrophotometers; Mindray Biochem FC) chemistry analyzers. All reagents utilized were certified for human studies (Sigma-Aldrich and PanReac AppliChem). Enzyme-linked immunosorbent assays (ELISAs) were carried out using commercial kits in strict accordance with the manufacturers' protocols.

Statistical processing was performed using Statistica for Windows, version 6.0, and Epi Info 2000, version 3.3.2. Quantitative variables were expressed as M ± SD or medians with interquartile ranges. A comparative analysis used Student's t-test for normally distributed data and the Mann-Whitney U-test for nonparametric data. Qualitative characteristics were compared using Pearson's $\chi 2$ test. Relative risk (RR), odds ratio (OR), and attributable risk (AR) with a 95 % CI were calculated for gender-associated risks. A value of $p<0.05$ was considered statistically significant.

All figures, illustrations, and clinical photographs included in this manuscript are original and were captured/created by the authors specifically for this study.

Results of the study. Gender distribution analysis revealed a significant female predominance (65.4 % vs. 34.6 %, $p<0.05$). Our statistical evaluation demonstrated a significant relative risk (1.31 (95 % CI:1.01–1.69), $p<0.05$) and odds ratio (1.89 (95 % CI:1.03–3.48), $p<0.05$) for the development of LS in women, with an attributable risk of 50.0 % compared to men.

While young patients (under 20) accounted for 15.4 % of the cohort, the highest prevalence was recorded among elderly patients (55–70 years), comprising 43.6 % of the sample. Our cross-classification by sex and age showed that disease onset in men occurred significantly more often before age 20 (22.2 %) compared to women ($p<0.05$). Conversely, in age groups over 55, women significantly predominated (56.8 % vs. 18.5 %), indicating that a postmenopausal onset is a defining feature of this pathology in female patients (Table 1).

Table 1

Distribution of patients with LS by age groups (n=78)

Age	ABS	%
up to 20 years	12	15.4
20-35 years	7	9.0
35-55 years	18	23.0
55-70 years	34	43.6
over 70 years	7	9.0

Regarding disease duration, 51.3 % of patients had symptoms for 2 to 6 years, and 21.8 % received a verified diagnosis within the first 2 years. The most frequently reported trigger was psycho-emotional stress (38.5 %), followed by occupational hazards (19.2 %), cold exposure (15.4 %), and acute respiratory viral infections (15.4 %).

In our study, comorbidities were diagnosed in 44.9 % of patients, with hypertension (20.5 %), gastrointestinal disorders (17.9 %), and diabetes mellitus (10.3 %) being the most common.

Clinical progression of LS follows three stages: initial edema, induration/sclerosis, and terminal atrophy. Morphea is characterized by extreme clinical diversity (Fig. 1).

Superficial forms are often accompanied by itching and pain, while linear scleroderma – especially in children – can lead to muscle spasms, limb length discrepancies, and permanent disability (Fig. 2). The negative impact on daily life significantly increases the predisposition to anxiety and depression.

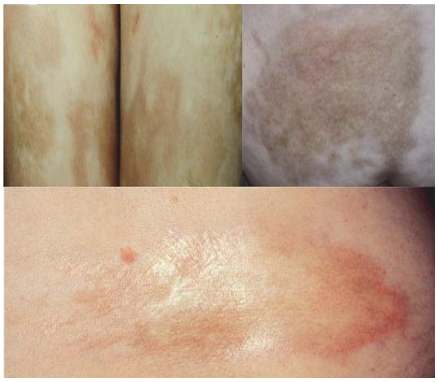


Fig. 1. Subforms of localized scleroderma.

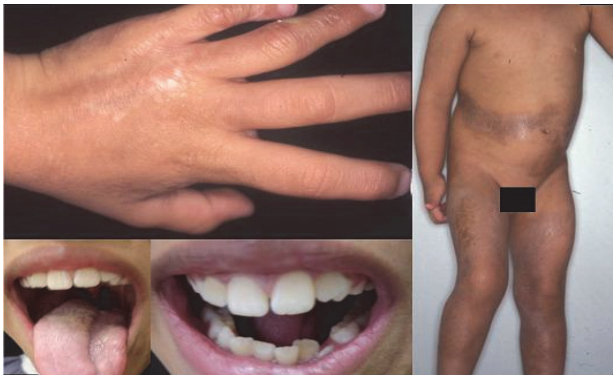
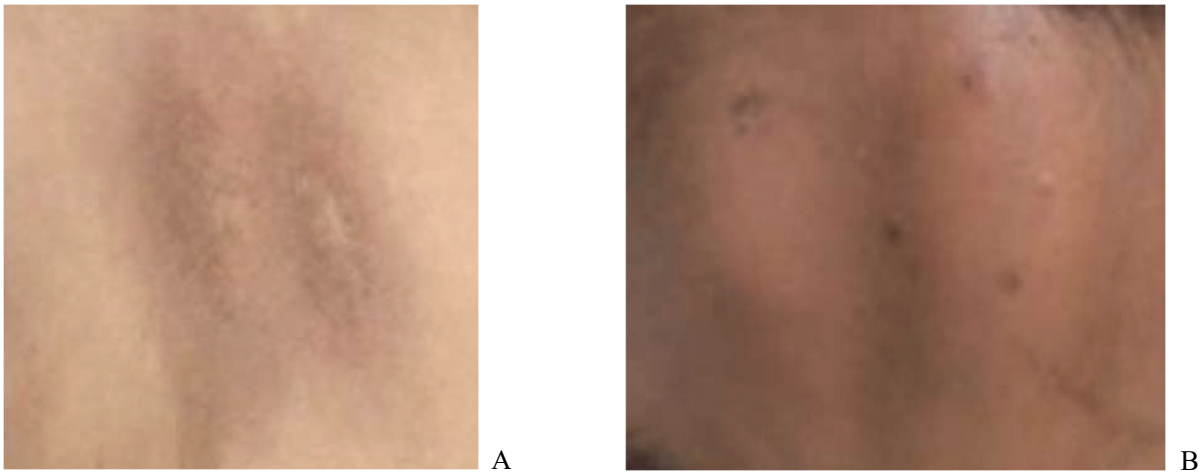


Fig. 2. Subforms of localized scleroderma in kids.

The diagnosis is primarily established on clinical examination and medicalhistory and is often confirmed by a skin biopsy. To ensure diagnostic accuracy and the development of a prognostic model, the following criteria were used: clearly defined sclerodermic skin changes; histopathological evidence of thickened dermal collagen fibers; and the differential exclusion of systemic scleroderma, eosinophilic fasciitis, lichen sclerosus et atrophicus, keloids, and sclerosing panniculitis.

Among the patients we studied, the majority of cases – 55 (70.5 %) – consisted of the plaque form (Fig. 3A). In a number of cases, the linear form was observed, which ranked second in frequency – 12 cases (12 persons, 15.4 %) (Fig. 3B). In some patients, lichen sclerosus et atrophicus of Zumbusch (7 persons, 9.0 %) and idiopathic atrophoderma of Pasini-Pierini (4 persons, 5.1 %) were diagnosed. Rarer forms of LS, such as lichen sclerosus et atrophicus and idiopathic atrophoderma of Pasini-Pierini, are considered adult forms and are characteristic of patients aged 30–40 years.



A B

Fig. 3. A – Plaque form of localized scleroderma, B – Linear form of localized scleroderma.

Analysis of the lesions in patients included in the study made it possible to determine the stages of the skin process: the majority of patients (47 individuals, 61.0 %) had the induration stage, while individual patients had the atrophy stage (6 individuals, 8.0 %), which indicates late diagnosis of the disease. The number of skin lesions ranged from 1 to 5 (average number of foci: 2.8±1.12), indicating that LS more often had a multifocal course.

The clinical manifestations of the dermatosis developed in a specific sequence, allowing distinction among the following stages: progressive (50 individuals, 64.0 %), stabilization (20 individuals, 25.6 %), and regression (8 individuals, 10.2 %). Among patients with progressive LS, the plaque form predominated (49 individuals, 98.0 %), and 1 individual (2.0 %) presented with the linear form. During stabilization, the linear form (5 individuals, 25.0 %), lichen sclerosus et atrophicus (6 individuals, 30.0 %), idiopathic atrophoderma (3 individuals, 15.0 %), and the plaque form (6 individuals, 30.0 %) were detected. During regression, rarer forms of LS were more frequently diagnosed: the linear form (6 individuals, 75.0 %), lichen sclerosus et atrophicus (1 individual, 12.5 %), and idiopathic atrophoderma (1 individual, 12.5 %).

In this article, we paid special attention to the assessment of endothelial dysfunction using vascular endothelial growth factor (VEGF), as it is a key regulator of angiogenesis, the expression of which increases under conditions of tissue hypoxia and ischemia, and can serve as a prognostic marker for the severity of the LS course. In patients with systemic and localized scleroderma, this marker reflects the dysregulation of vascular growth and the development of microangiopathies. In our study, a statistically significant ($p<0.05$) increase in VEGF-A levels was observed in patients with localized scleroderma: primary group: 445.9 (218.5–644.9) pg/mL; control group: 96.6 (99.3–110.4) pg/mL. The data confirm significant activation of endothelial proliferation in this pathology.

Assessment of gender dependence showed a higher VEGF-A content (16.0 %) in female patients – 418.8 (179.6–629.9) pg/mL – compared with male patients – 361.1 (110.4–454.4) pg/mL.

A U-shaped age dependence of the disease course should also be noted: a high VEGF-A content was found in patients under the age of 20 years – 424.3 (229.3–662.9) pg/mL, with a significant decrease in the angiogenic factor by 2.82 times among patients aged 20–35 years – 150.3 (77.5–163.7) pg/mL, and a subsequent increase by 2.62 times among patients aged 35 to 55 years – 393.6 (108.8–703.9) pg/mL. The maximum vascular endothelial growth factor content in LS was observed in patients aged 55 years or older – 490.0 (226.9–659.9) pg/mL, $p<0.05$.

Upon evaluating the content of vascular endothelial growth factor in various cutaneous forms of localized scleroderma, it was revealed that the highest marker content was observed in the classic plaque-like form – 487.9 (226.9–684.4) pg/mL ($p<0.05$) and the lowest in idiopathic atrophoderma of Pasini-Pierini – 251.2 (195.0–320.2) pg/mL ($p<0.05$), with no reliable difference in lichen sclerosus et atrophicus (320.9 (109.8–531.9) pg/mL) and linear scleroderma (374.3 (163.6–454.4) pg/mL).

The VEGF-A level was 28.2 % higher when skin lesion involvement exceeded 5.0 % (499.0 (391.0–1249.0) pg/mg) compared to the VEGF-A content when skin lesion involvement was up to 5.0 % (389.1 (354.9–871.3) pg/mg), $p<0.05$.

A similar dependence was observed during analysis of vascular endothelial growth factor (VEGF) content according to disease severity – in mild involvement, the VEGF-A level reached 381.1 (246.5–658.6) pg/mL. In the moderate course, VEGF-A content was 463.8 (329.7–827.9) pg/mL, which was 21.7 % higher than in the mild course group ($p<0.05$).

Discussion. Our findings on the demographic, clinical, and biochemical profiles of patients with localized scleroderma closely align with the current literature. The significant female predominance observed in our cohort is consistent with other reports indicating that the pathology is more frequently diagnosed in females, with a female-to-male ratio of 2.6–6:1 [4]. The postmenopausal peak observed in our study is corroborated by Andersen L. K. et al., who reported an increase in scleroderma hospitalizations among women over 50, possibly linked to unknown infectious, allergic, or demographic factors [1].

Similarly, the prevalence of associated diseases in our patients reflects general trends in scleroderma management. While we recorded high frequencies of hypertension and gastrointestinal disorders, Bali G. et al. reported other significant comorbidities such as dyslipidemia (18.4 %), diabetes (5.6 %), and osteoporosis (24 %) in scleroderma patients [3].

In terms of clinical presentation, our observation that the plaque form constitutes the majority of cases is supported by Moinzadeh P. et al., who note that plaque scleroderma is indeed the most common form of LS and occurs more frequently in adult patients [9]. They also emphasize that rarer forms of LS, such as lichen sclerosus et atrophicus and idiopathic atrophoderma of Pasini-Pierini, are considered adult forms and are characteristic of patients aged 30–40 years, which aligns with the diverse manifestations recorded in our sample.

Finally, assessment of endothelial dysfunction using VEGF-A provides robust biochemical confirmation of microangiopathy in LS. Our finding of significantly elevated VEGF-A levels is supported by similar results from another study, which demonstrated increased vascular endothelial growth factor [7]. Moreover, the relationship we established between VEGF-A levels and disease severity is consistent with findings by Shenavandeha S. et al., who report a correlation between VEGF levels and the extent of skin induration [13].

Thus, increasing diagnostic accuracy is a fundamental prerequisite for optimizing treatment outcomes and mitigating the long-term consequences of localized scleroderma. Based on the provided research results, statistical data, and biomarker analysis, we have developed a prognostic model for the diagnosis and course of LS. This model integrates clinical, demographic, and laboratory parameters to determine risk group and predict disease severity.

A. Stage of primary risk stratification (Anamnestic).

– Gender factor: Women have a 1.89 times higher risk of developing LS ($p<0.05$).

– Age determinant: Peak risk group: 55–70 years (especially for postmenopausal women);

– Early onset risk group: Males under 20 years of age.

– Trigger screening and comorbidity: History of psycho-emotional stress (38.5 %), hypothermia, past acute respiratory viral infections, cardiovascular and endocrine disorders.

B. Stage of clinico-morphological verification.

– Typology: Priority attention to the plaque form (70.5 %).

–Staging: Detection of the induration (thickening) stage indicates an active pathological process, while the atrophy stage indicates the need for consequence correction.

–Prevalence: Involvement of >5 % of the body surface area is associated with an aggressive course.

C. Stage of laboratory-prognostic modeling (VEGF-A Marker). The VEGF-A level serves as a key indicator of angiogenesis activity and fibrosis severity:

– Normal threshold: ≈ 100 pg/mL.

–Prognosis of moderate severity/progression: VEGF-A level >450 pg/mL.

– Correlation with form: The highest values are expected in the plaque form (average 487.9 pg/mL).

– U-shaped prognosis: High VEGF-A levels in patients <20 years and >55 years indicate increased endothelial proliferative activity in these age groups.

Thus, the diagnosis of localized scleroderma should be based on the synthesis of clinical morphology, history of lesion evolution, and instrumental screening to exclude systemic overlap.

Limitations. The limitations of this work are the small sample size (n=78) within a single center and the short six-month observation period, which, together with the absence of dynamic monitoring of the VEGF-A level, the lack of high-frequency skin ultrasound, and the non-randomized design, limit the ability to assess long-term recurrences and broadly generalize the results.

Conclusion

A significant gender disproportion was established in the prevalence of localized scleroderma, with a predominance of women (65.4 %, OR=1.89). Two age peaks of activity were identified: a juvenile-onset peak in males (under 20 years of age) and a postmenopausal peak in females (55–70 years), which must be considered when developing diagnostic algorithms. The plaque form remains the most common LS subtype (70.5 %). The high frequency of detecting patients in the induration stage (61.0 %) and progressive phase (64.0 %) indicates the insufficient effectiveness of early diagnosis at the erythema stage, which leads to irreversible dermal changes.

It has been proven that vascular endothelial growth factor (VEGF-A) is an objective marker of LS severity. Its level in patients (445.9 pg/mL) is almost 4.5 times higher than that of healthy individuals. A direct correlation was established between VEGF-A concentration and the area of skin involvement (>5 %) and the severity of the clinical course, allowing the use of this parameter for monitoring disease activity. Psycho-emotional stress was identified as the main trigger factor of the disease (38.5 %). The high level of concomitant pathology (44.9 %), particularly cardiovascular and endocrine disorders, emphasizes the need for a multidisciplinary approach to the management of patients with LS. The peak incidence of LS is observed in the 55–70-year age group (43.6 %), which warrants increased clinical vigilance during dermatological screening of this demographic. Males have a significantly higher risk profile (OR 1.89) than females in the studied population, underscoring the need to account for gender differences in diagnostic protocols. Comprehensive treatment plans must be justified by the established diagnosis and consider systemic concomitant diseases to ensure optimal treatment outcomes for patients.

Prospects for further research. Future research should focus on validating our prognostic model through larger, multicenter studies with longer follow-up periods. It is essential to track VEGF-A levels over time—especially before and after treatment – to confirm its reliability in predicting disease relapses. Additionally, combining this blood marker with non-invasive tools like high-frequency skin ultrasound will help correlate physical skin changes with internal vascular data in real time. Finally, investigating how stress triggers the condition, and why it frequently co-occurs with heart and endocrine disorders, will be key to developing better, well-rounded patient care.

References

1. Andersen LK, Davis MDP. Prevalence of Skin and Skin-Related Diseases in the Rochester Epidemiology Project and a Comparison with Other Published Prevalence Studies. Dermatology. 2016;232(3):344–52.doi: 10.1159/000444580.
2. Asano Y, Fujimoto M, Ishikawa O, Sato S, Jinnin M, Takehara K, et al. Diagnostic criteria, severity classification and guidelines of localized scleroderma. The Journal of Dermatology. 2018 Apr;45(7):755–80.doi: 10.1111/1346-8138.14161.
3. Bali G, Szilvási A, Inotai D, Varga Á, Sárdy M, Kárpáti S, et al. Comorbidity of localized scleroderma and primary biliary cholangitis. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2018 Nov;16(11):1323–7. doi: 10.1111/ddg.13693.
4. Calderon LM, Pope JE. Scleroderma epidemiology update. Curr Opin Rheumatol. 2021;33(2):122-127. doi:10.1097/BOR.0000000000000785.
5. Distler O, Cozzio A. Systemic sclerosis and localized scleroderma: current concepts and novel targets for therapy. Seminars in Immunopathology. 2016;38(1):87–95. doi:10.1007/s00281-015-0520-3.
6. George R, George A, Kumar TS. Update on Management of Morphea (Localized Scleroderma) in Children. Indian Dermatology Online Journal [Internet]. 2020 Mar 9 [cited 2021 May 26];11(2):135–45. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7247622/.
7. Li Z, Xiao Y, Kang L, et al. Comparative Study of Adipose-Derived Stem Cells from Localized Scleroderma Patients and Healthy Donors in Treating Skin Fibrosis. Plast Reconstr Surg. 2025;155(4):716e-726e. doi:10.1097/PRS.0000000000011779.
8. Kreuter A, Moinzadeh P, Kinberger M, et al. S2k guideline: Diagnosis and therapy of localized scleroderma. J Dtsch Dermatol Ges. 2024;22(4):605-620. doi:10.1111/ddg.15328.
9. Moinzadeh P, Hunzelmann N, Kreuter A, Krieg T. Localized scleroderma: a review. Journal of Scleroderma and Related Disorders. 2016;1(3):286–97.https://doi.org/10.5301/jsrd.5000215.
10. Penmetsa GK, Sapra A. Morphea [Internet]. PubMed. Treasure Island (FL): StatPearls Publishing; 2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559010/.
11. Rodríguez-Salgado P, García-Romero MT. Morphea: a practical review of its diagnosis, classification and treatment. Gac Med Mex. 2019;155(5):483-491. doi:10.24875/GMM.M20000336
12. Rongioletti F, Ferreli C, Atzori L, Bottoni U, Soda G. Scleroderma with an update about clinico-pathological correlation. G Ital Dermatol Venereol. 2018;153(2):208-215. doi:10.23736/S0392-0488.18.05922-9.
13. Shenavandeha S., Eskandar T. T., Nazariniaad K. S. M. Serum vascular endothelial growth factor (VEGF), soluble VEGF receptor-1 (sVEGFR-1) and sVEGFR-2 in systemic sclerosis patients: Relation to clinical manifestations and capillaroscopy findings. The Egyptian Rheumatologist. 2017; 39 (1): 19-24.
14. Tsou Pei Suen, Sawalha AH. Unfolding the pathogenesis of scleroderma through genomics and epigenomics. Journal of Autoimmunity [Internet]. 2017 Sep;83:73–94. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5573604/.
15. Zhao M, Wu J, Wu H, Sawalha AH, Lu Q. Clinical Treatment Options in Scleroderma: Recommendations and Comprehensive Review. Clin Rev Allergy Immunol. 2022;62(2):273-291. doi:10.1007/s12016-020-08831-4.

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