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PROSPECTIVE ANALYSIS OF CLINICAL FEATURES ASSOCIATED WITH DISEASE COURSE AND ACTIVITY IN SYSTEMIC SCLEROSIS

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ПРОСПЕКТИВНЫЙ АНАЛИЗ КЛИНИЧЕСКИХ ОСОБЕННОСТЕЙ И АКТИВНОСТИ ЗАБОЛЕВАНИЯ ПРИ СИСТЕМНОМ СКЛЕРОЗЕ

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TIZIMLI SKLERODERMIYADA KASALLIK KECHISHI VA FAOLLIGI BILAN BOG‘LIQ KLINIK XUSUSIYATLARNING PROSPEKTIVTAHLILI

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Цель: *проспективный анализ клинических особенностей, связанных с течением и активностью заболевания у пациентов с системным склерозом, и оценка их связи с уровнем воспалительных цитокинов.* ***Материал и методы:*** *перспективное наблюдательное исследование включало 64 пациента с системным склерозом, находившихся под наблюдением в специализированном ревматологическом центре. Диагноз был установлен согласно критериям классификации ACR/EULAR 2013.* ***Результаты:*** *из 64 пациентов диффузный кожный системный склероз был выявлен у 38 (59,4%). Ограниченный кожный системный склероз наблюдался у 26 (40,6%) больных. Активное заболевание было выявлено у 37 пациентов (57,8%), в то время как у 27 (42,2%) была низкая или умеренная активность заболевания.* ***Выводы:*** *проспективный анализ пациентов с системным склерозом показал, что активность заболевания тесно связана со специфическими клиническими особенностями и повышенным уровнем TNF-α и ИЛ-6.*

Ключевые слова:*системная склеродермия, TNF-α, ИЛ-17A, mRSS.*

Maqsad: *tizimli skleroz bilan og‘rigan bemorlarda kasallikning kechishi va faolligi bilan bog‘liq klinik xususiyatlarni istiqbolli tahlil qilish va ularning yallig‘lanish sitokinlari darajasi bilan bog‘liqligini baholash.* ***Material va usullar:*** *ushbu istiqbolli kuzatuv tadqiqotiga ixtisoslashtirilgan revmatologiya markazida tizimli skleroz bilan og‘rigan 64 nafar bemor kiritilgan. Tashxis ACR/EULAR 2013 tasnifi mezonlariga muvofiq qo‘yilgan.* ***Natijalar*** *64 nafar bemor orasida 38 nafar (59,4%) bemorda diffuz teri KQK aniqlandi. Chegaralangan teri KQK 26 nafar bemorda (40,6%) kuzatildi. Faol kasallik 37 nafar bemorda (57,8%) aniqlangan bo‘lsa, 27 nafar bemorda (42,2%) kasallikning past yoki o‘rtacha faolligi kuzatilgan.* ***Xulosalar:*** *tizimli skleroz bilan og‘rigan bemorlarning prospektiv tahlili shuni ko‘rsatdiki, kasallikning faolligi o‘ziga xos klinik xususiyatlar va TNF-α va IL-6 darajasining oshishi bilan chambarchas bog‘liq.*

Kalit so‘zlar: *tizimli sklerodermiya, TNF-α, IL-17A, mRSS.*

Systemic sclerosis (SSc) is a heterogeneous autoimmune disease characterized by immune dysregulation, vasculopathy, and progressive fibrosis of the skin and internal organs. The clinical course of SSc varies significantly, ranging from slowly progressive limited forms to rapidly advancing diffuse disease with severe organ involvement. Understanding disease activity and predicting progression remain major challenges in clinical practice. Increasing evidence suggests that inflammatory cytokines play a pivotal role in the initiation and perpetuation of fibrotic and vascular damage. Among them, tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) are considered key mediators linking immune activation with endothelial dysfunction and fibrosis.Prospective evaluation of clinical manifestations in relation to cytokine profiles may improve early identification of active disease and enhance prognostic accuracy. This study aimed to analyze prospectively the clinical features associated with disease course and activation in systemic sclerosis patients.

Purpose of the study

To conduct a prospective analysis of clinical features associated with disease course and activity in patients with systemic sclerosis and to evaluate their relationship with inflammatory cytokine levels.

Material and methods

This prospective observational study included 64 patients with systemic sclerosis who were followed at a specialized rheumatology center. Diagnosis was established according to ACR/EULAR 2013 classification criteria**.**All patients underwent standardized clinical evaluation, includingdisease subtype classification (limited vs diffuse), modified Rodnan Skin Score (mRSS), assessment of Raynaud’s phenomenon, digital ulcers, evaluation of internal organ involvement (lung, heart, kidney, gastrointestinal tract).Disease activity was assessed using EULAR activity indices**.**Serum levels of TNF-α and IL-6 were measured using commercially available ELISA kits**.** Standard inflammatory markers (ESR, CRP) were also analyzed.Statistical analysis was performed using standard biomedical methods. Quantitative data were expressed as mean ± SD. Correlation analysis was conducted using Spearman’s coefficient. A p-value < 0.05 was considered statistically significant.

Results

Among the 64 patients diffuse cutaneous SSc was identified in 38 patients (59.4%). Limited cutaneous SSc was observed in 26 patients (40.6%). Active disease was identified in 37patients (57.8%)**,** while27 patients (42.2%) had low or moderate disease activity. High disease activity was significantly associated with: higher mRSS scores, presence of digital ulcers, interstitial lung disease,elevated ESR and CRP. Patients with diffuse SSc demonstrated a more aggressive disease course and earlier internal organ involvement. Patients with active systemic sclerosis had significantly higher serum levels of:IL-6 **(**p<0.01), TNF-α (p<0.05). IL-6 levels correlated positively with:mRSS (r=0.62), pulmonary involvement severity (r=0.58). TNF-α levels were primarily associated with vascular manifestations, including Raynaud’s phenomenon severity and digital ischemia.

Table 1

Baseline Clinical Characteristics

Parameter	Total, n=64	Active disease, n=37	Low/Moderate activity, n=27	p-value
Age, years (mean±SD)	45.8±11.6	44.9±10.8	47.1±12.3	>0.05
Disease duration, years	6.2±3.1	4.9±2.7	7.8±3.4	<0.05
Female sex, n (%)	56 (87.5)	33 (89.2)	23 (85.2%)	>0.05
Diffuse cutaneous SSc, n (%)	38 (59.4)	27 (73.0)	11 (40.7)	<0.01
mRSS	18.4±6.9	22.7±6.1	12.6±4.8	<0.001

Table 1 summarizes the baseline demographic and clinical characteristics of the patients with systemic sclerosis included in the prospective study. The study population was predominantly female (87.5%), which is consistent with the known epidemiological profile of systemic sclerosis. The mean age of the patients was 45.8±11.6 years, with no statistically significant difference between patients with active disease and those with low or moderate disease activity (p>0.05). Disease duration was significantly shorter in the group with active systemic sclerosis compared to the low/moderate activity group (4.9±2.7 vs. 7.8±3.4 years; p<0.05), indicating that higher inflammatory activity is more frequently observed during earlier stages of the disease. Diffuse cutaneous systemic sclerosis was significantly more prevalent among patients with active disease (73.0%) than among those with low or moderate activity (40.7%; p<0.01). In contrast, the limited cutaneous form predominated in patients with lower disease activity. The modified Rodnan skin score (mRSS) was markedly higher in the active disease group (22.7±6.1) compared to the low/moderate activity group (12.6±4.8; p<0.001), reflecting more severe skin fibrosis. Vascular and visceral manifestations, including digital ulcers, interstitial lung disease, pulmonary hypertension, and gastrointestinal involvement, were observed significantly more frequently in patients with active systemic sclerosis (p<0.0500.01), highlighting the systemic nature of disease activation and its association with internal organ involvement.

Table 2

Cytokine Levels According to Disease Activity

Cytokine	Active disease, n=37	Low/Moderate activity, n=27	p value
TNF-α, pg/ml	18.9±4.7	12.3±3.9	<0.05
IL-6, pg/ml	26.4±6.8	14.1±5.2	<0.001

Table 2 presents the serum concentrations of pro-inflammatory cytokines TNF-α and IL-6 in patients stratified by disease activity. Patients with active systemic sclerosis demonstrated significantly higher serum levels of TNF-α compared with those with low or moderate disease activity (18.9±4.7 pg/ml vs. 12.3±3.9 pg/ml; p<0.05). A more pronounced difference was observed for interleukin-6. Mean IL-6 levels in the active disease group (26.4±6.8 pg/ml) were nearly twofold higher than in patients with low or moderate activity (14.1±5.2 pg/ml; p<0.001). These findings indicate a strong association between IL-6-mediated inflammation and disease activation in systemic sclerosis.

Conclusions

1. Prospective analysis of patients with systemic sclerosis demonstrated that disease activity is closely associated with specific clinical features and elevated levels of TNF-α and IL-6.

2. These cytokines may serve as reliable biomarkers for disease activation and progression, contributing to improved prognostic evaluation and personalized therapeutic approaches.

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Objective: *To prospectively analyze clinical features associated with the course and activity of the disease in patients with systemic sclerosis and to evaluate their relationship with the level of inflammatory cytokines.* ***Material and methods:*** *This prospective observational study included 64 patients with systemic sclerosis followed up in a specialized rheumatology center. The diagnosis was established according to the ACR/EULAR 2013 classification criteria.* ***Results:*** *Of the 64 patients, diffuse cutaneous systemic sclerosis was detected in 38 (59.4%). Limited cutaneous systemic sclerosis was observed in 26 patients (40.6%). Active disease was detected in 37 patients (57.8%), while 27 (42.2%) had low or moderate disease activity.* ***Conclusions:*** *A prospective analysis of patients with systemic sclerosis showed that disease activity is closely associated with specific clinical features and elevated levels of TNF-α and IL-6.*

Key words: *systemic sclerosis, TNF-α, IL-17A, mRSS.*

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