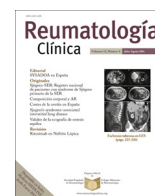




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Brief report

Clinical phenotype and outcome in lupus according to age: a comparison between juvenile and adult onset



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ABSTRACT

Objective: To study differences in demographic, clinical and immunologic characteristics, activity and cumulative organ damage according to age of onset in systemic lupus erythematosus (SLE).

Methods: Cross-sectional study was performed including 204 SLE patients. Characteristics were compared between juvenile and adult-onset SLE patients using parametric and nonparametric tests (SPSS 23.0).

Results: Juvenile-SLE patients had malar rash more often (78.9% vs 53%; $p=0.001$), oral ulcers (45.5% vs 17.5%; $p=0.001$), neurological involvement (13.1% vs 3.6%; $p=0.02$) nephritis (50% vs 33.9%; $p=0.04$) and haematological manifestations such as hemolytic anaemia (23.6% vs 5.4%; $p=0.002$) and leukopenia (46.1% vs 4.2%; $p<0.001$). Arthritis was more prevalent in adult-onset patients (70.9% vs 90%; $p<0.04$). Overall, 20% of juvenile patients had chronic damage (Systemic Lupus International Collaborating Clinics/Damage Index [SLICC/DI] ≥ 1). However, the percentage of patients with irreversible damage was higher in the adult SLE patient group (24%, $p=0.04$). No statistically significant differences were found in other characteristics studied.

Conclusion: In summary, our study confirms the existence of differences in clinical manifestations, according to age at diagnosis of SLE. Juvenile-SLE patients showed a more aggressive clinical presentation.

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Fenotipo clínico y resultado en el lupus de acuerdo con la edad: una comparación del lupus de comienzo juvenil y lupus del adulto

RESUMEN

Objetivo: Estudiar las diferencias en las características demográficas, clínicas, inmunológicas, en la actividad y daño crónico de acuerdo con la edad de aparición del lupus eritematoso sistémico (LES).

Métodos: Se realizó un estudio de corte transversal incluyendo 204 pacientes con LES. Las características se compararon entre los pacientes con lupus de comienzo juvenil y del adulto utilizando testes paramétricos y no paramétricos (SPSS 23.0).

Resultados: Los pacientes con LES juvenil tenían más frecuentemente rash malar (78,9 vs. 53%; $p=0.001$), úlceras orales (45,5 vs. 17,5%; $p=0.001$), afectación neurológica (13,1 vs. 3,6%; $p=0.02$) nefritis (50 vs. 33,9%, $p=0.04$) y las manifestaciones hematológicas como anemia hemolítica (23,6 vs. 5,4%; $p=0.002$) y leucopenia (46,1 vs. 4,2%; $p<0.001$). La artritis era más frecuente en los pacientes con lupus del adulto (70,9 vs. 90%; $p=0.04$). El 20% de los pacientes juveniles tenían daño crónico (Systemic Lupus International Collaborating Clinics/Damage Index [SLICC/DI] ≥ 1). Sin embargo, el porcentaje de pacientes con daño irreversible fue superior en adultos (24%, $p=0.04$). No se encontraron diferencias estadísticamente significativas en relación con las otras características estudiadas.

Conclusión: En resumen, nuestro estudio confirma la existencia de diferencias en las manifestaciones clínicas según la edad al momento del diagnóstico del LES. Pacientes con LES de comienzo juvenil mostraron una presentación clínica más agresiva.

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Background

Systemic lupus erythematosus (SLE) is a severe, multi-systemic rheumatic disease. It is most prevalent among women of childbearing age, but can occur in all ages. In about 10–20% of cases it begins before 16 years.^{1,2}

Several studies have reported that age at onset has a modifying effect on disease expression. Juvenile-onset SLE (jSLE) tends to have a more aggressive presentation and course, high rates of organ involvement and increased need for long-term immunosuppressive medications.^{3–5}

Most studies have found a higher prevalence of lupus nephritis and haematological involvement in jSLE. Among adults, mild forms prevail, being the discoid lupus and arthritis more common in this group. However, in respect of many other clinical manifestations, including neuropsychiatric lupus (NPSLE), serositis, and autoantibody profiles, reports are conflicting, which is probably due to the small number of patients analysed in these studies.^{4–7}

These observations are of high importance since a high prevalence of severe organ involvement, as well as an early and prolonged exposure to high dose of steroid therapy and immunosuppressive drugs, raises concerns regarding the long-term morbidity and early mortality.

Although patients with jSLE present more often with severe forms of disease, differences in cumulative long-term damage, according to age of onset, is not well known. Few studies have proved the existence of a greater cumulative damage juvenile SLE patients. In 2008, Tucker and colleagues found a higher renal damage in these patients. In the same year, Ramirez Gomez and colleagues and Brunner and colleagues, showed that juvenile SLE patients had higher rates of activity (assessed by SLEDAI) but also may a higher chronic damage (assessed by SLICC/ACR index).^{8–10}

The objectives of the study were to compare patients with juvenile-onset SLE with those with adult-onset subset, regarding demographic, clinical and immunologic manifestations and to compare the cumulative organ damage between the groups.

Patients and methods

Cross-sectional study was performed.

Patients

204 consecutive patients with diagnosis of SLE (according to the American College of Rheumatology 1997 criteria¹¹), followed in our Rheumatology department of a tertiary University Hospital from Portugal, were included. Two groups were compared according to age of onset: juvenile and adult SLE. Juvenile-onset SLE was considered in those patients who began their disease at age of 16 or before.

No additional samples or outpatient attendances were required from patients for study purposes, thus ethical approval and informed consent were not required.

Clinical data

Demographic, clinical and immunological data were retrospectively obtained by consulting the clinical records and the national database Reuma.pt. The following variables were collected: gender, age at diagnosis, ethnicity, duration of follow-up, clinical manifestations including malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, nephritis, neuropsychiatric involvement, haemolytic anaemia, leukopenia, thrombocytopenia and autoantibodies (antinuclear antibodies (ANA), anti-double stranded DNA antibody (anti-DsDNA), anti-Smith antibody (anti-Sm), lupus anticoagulant and anti-cardiolipin antibodies). Autoantibodies were

considered positive if the value was above the cut-offs for the laboratory at least in one determination during the follow-up period, except for anti-cardiolipin antibodies, which were considered present if there was two positive doseaments apart from twelve weeks.

Disease activity was calculated using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and assessment of chronic organ damage was performed with the Systemic Lupus International Collaborative Clinics/American College of Rheumatology (SLICC/ACR) Damage Index. Both indexes were calculated in the last visit.

Statistical analysis

Demographic, clinical and immunological variables were compared between two groups according to age at diagnosis: jSLE (≤ 16 years) and adult-onset lupus (>16 years).

Continuous variables are expressed as mean and standard deviation, if they have a normal distribution, or median and range, if distribution is highly skewed. Kolmogorov–Smirnov test was used to verify the normal distribution of continuous variables. Categorical variables are presented as absolute values and percentages.

For continuous variables, values were compared using Student's *t*-test or Mann–Whitney test depending on normality distribution of variables. Categorical variables were analysed Fisher exact test.

The level of significance was set at 0.05. All statistical analyses were performed using SPSS, version 23.0.

Results

A total of 204 patients diagnosed with SLE were included, comprising 38 (18.6%) jSLE and 166 (81.4%) adult-onset SLE patients. 187 (91.7%) patients were female and had a mean age of 46.1 ± 15.4 years and a mean of disease duration of 17.1 ± 10 years (Table 1).

The most prevalent clinical manifestations in this cohort of SLE patients were: arthritis (88.2%) and muco-cutaneous

Table 1

Demographic, clinical and immunological characteristics of the 204 SLE patients included.

Characteristic	
Juvenile lupus, n (%)	38 (18.6)
Adult-onset lupus, n (%)	166 (81.4)
Female gender, n (%)	187 (91.7)
White race, n (%)	203 (99.5)
Age at diagnosis, mean \pm SD	30.3 \pm 13.7
Disease duration, mean \pm SD	17.1 \pm 10
<i>Clinical manifestations, n (%)</i>	
Malar rash	118 (57.8)
Photosensitivity	149 (73)
Discoid rash	13 (6.4)
Oral ulcers	46 (22.5)
Arthritis	180 (88.2)
Serositis	29 (14.1)
Nephritis	82 (40.2)
CNS involvement	11 (5.4)
Haematological involvement	84 (41.2)
<i>Immunological manifestations, n (%)</i>	
ANA positive	204 (100)
Anti-dsDNA positive	189 (92.6)
Anti-Sm positive	33 (16.2)
Lupus anticoagulant positive	33 (16.2)
IgG/IgM anticardiolipin positive	28 (13.7)
IgM/IgG anti-B2GPpositive	26 (12.7)

SD, standard deviation; CNS, central nervous system; ANA, antinuclear antibodies; anti-DsDNA, anti-double stranded DNA antibodies, anti-Sm, anti-Smith antibody; anti-B2GP, anti-beta 2 glycoprotein.

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