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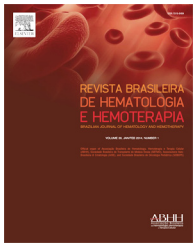

Original article

Prevalence of the American College of Rheumatology hematological classification criteria and associations with serological and clinical variables in 460 systemic lupus erythematosus patients

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ABSTRACT

Objective: To study systemic lupus erythematosus in a Brazilian population using the American College of Rheumatology hematological classification criteria and report associations of the disease with serological and clinical profiles.
Methods: This is a retrospective study of 460 systemic lupus erythematosus patients followed in a single rheumatologic center during the last 10 years. Hematological manifestations considered for this study were hemolysis, leukopenia, lymphocytopenia and thrombocytopenia.
Results: The cumulative prevalences of leukopenia, thrombocytopenia, lymphocytopenia and hemolytic anemia were 29.8%, 21.08%, 17.7% and 8.4%, respectively. A higher percentage of patients with hemolysis had anticardiolipin IgM (p-value = 0.002). Those with leukopenia had more lymphopenia (p-value = 0.02), psychosis (p-value = 0.01), thrombocytopenia (p-value <0.0001) and anti-double stranded DNA antibodies (p-value = 0.03). Patients with lymphopenia had more leukopenia (OR = 1.8; 95% CI = 1.01–3.29) and lupus anticoagulant antibodies (OR = 2.2; 95% CI = 1.16–4.39) and those with thrombocytopenia had more leukopenia (OR = 3.1; 95% CI = 1.82–5.44) and antiphospholipid syndrome (OR = 3.1; 95% CI = 1.28–7.87).
Conclusion: The most common hematological finding was leukopenia and the least common was hemolysis. Associations of low platelet count and hemolysis were found with antiphospholipid syndrome and anticardiolipin IgM positivity, respectively. Leukopenia and lymphocytopenia are correlated and leukopenia is more common in systemic lupus erythematosus patients with psychosis, thrombocytopenia and anti-double stranded DNA.

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Introduction

Systemic lupus erythematosus (SLE), a systemic autoimmune disease most common in young females, has a very heterogeneous clinical profile.[1] The genetic background of patients affects not only the prevalence of SLE but also the phenotype.[2] Accordingly ethnic features favor the appearance of autoantibodies and clinical clusters that define the subtypes of the disease.[3,4] These aspects highlight the need to know lupus clusters as this awareness allows the clinician to predict a future manifestation from one already present. It also highlights the need for local knowledge of disease behavior, particularly in a population such as the Brazilian which is highly mixed from the ethnic point of view.

The classical hematological manifestations in SLE are hemolytic anemia, leukopenia, and thrombocytopenia; these manifestations are part of the 1997 revised American College Classification Criteria for SLE[5] as well as the new 2012 Systemic Lupus International Collaborating Clinics Classification Criteria.[6]

According to previous works, thrombocytopenia has a prevalence in the lupus population ranging from 7 to 30%.[7–9] Although thrombocytopenia is not directly associated with end organ damage, it defines a subgroup of patients with higher morbidity and consequently has important prognostic implications.[10]

Leukopenia is a typical feature of SLE and may occur as a result of lymphopenia, neutropenia or both.[11] Neutropenia, which may be mediated by anti-neutrophil antibodies, is common, with a prevalence in the order of 47%.[11,12] The prevalence of lymphopenia is variable, ranging from 20 to 81% and correlates with disease activity.[12,13] Both T and B lymphocytes are reduced while natural killer (NK) cells are elevated.[11,14] Although there are numerous reports of lymphocytotoxic antibodies,[11,15] their significance in this context remains uncertain. Reduced surface expression of complement regulatory proteins such as CD55 and CD59 has also been implicated in the pathogenesis of lupus lymphopenia, as this deficiency will make cells susceptible to complement-mediated lysis.[11,16]

Autoimmune hemolytic anemia (AIHA) is described in 7–15% of lupus patients and may occur together with immune thrombocytopenia in the Evans syndrome.[17,18] It is associated with the presence of warm (predominantly) and cold anti-red blood cell autoantibodies.[17]

The aim of the current study was to assess the prevalence of hematological manifestations in a cohort of Brazilian lupus patients as well as its associations with clinical and autoantibody profiles.

Methods

This is a retrospective study, approved by the local Research Ethics Committee. The charts of 460 SLE patients seen over the last 10 years in a single tertiary center were reviewed. To be included in this study, patients had to comply with at least four of the 1997 revised American College of Rheumatology classification criteria for SLE.[5] Patients diagnosed before the age of 16 years and those with incomplete records were excluded. Data on demographic, clinical and serological profile were obtained. The definition of all clinical findings followed those of the ACR classification criteria.[5] The criteria were cumulatively considered when the patient had no known infections. According to these criteria, hematological manifestations were defined as the presence of hemolytic anemia, leukopenia defined as less than 4×10^3 cells/mL on at least two occasions, lymphopenia defined as less than 1.5×10^3 cells/mL on at least two occasions and thrombocytopenia defined as less than 100×10^3 cells/mL in the absence of an offending drug.[5] Antiphospholipid syndrome (APS) was diagnosed according to the 2006 modified APS criteria.[19] The complete cell count was performed using an automated analyzer (XE2100D, Sysmex) and the white cell differential count was performed manually using Giemsa stain.

Statistical analysis

All obtained data were collected as frequencies in contingency tables. The Kolmogorov–Smirnov test was used to study data distribution. Groups of patients with one hematological manifestation (hemolytic anemia, leukopenia or thrombocytopenia) were compared with those without this particular manifestation in respect to other clinical manifestations and their autoantibody profile. Central tendency was expressed as median and interquartile range (IQR) when numeric data were nonparametric and mean and standard deviation (SD) when parametric. Association studies were performed by Fisher's exact and chi-square tests for nominal data and with Mann–Whitney and unpaired *t*-test for numerical data. All variables that had significance with a p-value <0.1 in univariate analysis, were further studied using logistic regression to assess independency. Statistical analyses were made using the Medcalc software version 10.0, and significance was set for an alpha error of 5%.

Results

Analysis of the sample

The sample was comprised of 93.5% females and 6.5% males with ages ranging from 16 to 88 years and median disease duration of 8 years. The clinic and serological profiles are listed in Table 1.

Study of lupus patients with hemolytic anemia

The comparison data of patients with and without hemolytic anemia (p-value <0.1) are shown in Table 2.

Association studies of hemolytic anemia with disease duration, age at diagnosis, gender, photosensitivity, oral ulcers, malar rash, discoid lesions, arthritis, glomerulonephritis, seizures, psychosis, serositis, lymphopenia, anti-Ro/SS-A, anti-La/SS-B, anti-ribonucleoprotein (anti-RNP), anti-double stranded DNA (anti-dsDNA), rheumatoid factor and APS were not significant.

On further investigating variables with p-values <0.1 in univariate analysis using a logistic regression model, only