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EVALUATION OF SLEDAI INFLAMMATORY ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS IN RELATION TO CHANGES IN THE WHITE AND RED SERIES OF THE BLOOD COUNT

Elizandra Hertel Lenhardt
University of Cuiabá, Faculty of Medicine
Cuiabá-MT
http://lattes.cnpq.br/7247953917565088

Marília Karoliny Gomes Bueno de Magalhães Bucair
University of Cuiabá, Faculty of Medicine
Cuiabá-MT
http://lattes.cnpq.br/2372855486034203

Verônica dos Santos Alves
University of Cuiabá, Faculty of Medicine
Cuiabá-MT
http://lattes.cnpq.br/8504781965714016

Izabella Gonzaga Gaspar
University of Cuiabá, Faculty of Medicine
Cuiabá-MT
http://lattes.cnpq.br/5140011327796387

Matheus Rafael Bueno Teixeira
University of Cuiabá, Faculty of Medicine
Cuiabá-MT
http://lattes.cnpq.br/5502056003569424

Susan Nunes Lindote
University of Cuiabá, Faculty of Medicine
Cuiabá-MT
http://lattes.cnpq.br/4541790172046318

Micheli Said de Marchi
University of Cuiabá, Faculty of Medicine
Cuiabá-MT
http://lattes.cnpq.br/3888494794674010

Abstract: Systemic lupus erythematosus (SLE) is a chronic, multisystem, autoimmune inflammatory disease characterized by an imbalance in the immune system, which causes damage to its own cells, causing damage throughout the body. Symptoms vary from fever, fatigue, joint pain, skin rashes (butterfly wings) to severe kidney, lung and heart damage. The etiology comprises a combination of genetic, hormonal, environmental and infectious factors. The aim of this study is to correlate the inflammatory activity of SLE using the *Systemic Lupus Erythematosus Disease Activity Index* (SLEDAI) with alterations in the white and red blood count. This is a retrospective longitudinal study using a repeated measures design, carried out between June 2010 and February 2014 at the General University Hospital (HGU) in Cuiabá-MT. With patients diagnosed with SLE according to the *American College of Rheumatology* (ACR) criteria, the data was analyzed using Pearson's correlation. There was a significant association between SLEDAI and red series, which showed a decrease in hemoglobin, hematocrit, VCM, HCM and CHCM. In addition, leukopenia, basopenia and lymphopenia were present in proportion to the increase in inflammatory activity, demonstrating a significant drop in immune defense cells. The database of results showed hematological alterations, characterized by microcytic and hypochromic anemia and greater susceptibility to infections due to the drop in the white series, positively correlating hematological alterations with the inflammatory activity of the disease and the action of autoantibodies. Therefore, the monitoring of patients with SLE must take into account these complex interactions between the disease and the hematological system, directing treatment strategies that are increasingly effective in controlling the disease and preventing damage to health.
Keywords: Lupus, SLEDAI, autoimmune, inflammation.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, multisystem, autoimmune inflammatory disease of unknown etiology, characterized by an imbalance in the immune system. It is caused by the presence of various autoantibodies and clinical manifestations that lead to dysfunction of the affected organ, impairing the quality of life and increasing the morbidity and mortality of sufferers (SOUZA, et al., 2021; CIURTIN, et al, 2024). It is a rare disease, with no cure, which most often affects young women between the second and third decade of life with an incidence of 4.8 to 8.7 cases per 100,000 inhabitants/year in Brazil, with a ratio of nine to ten women for every man. The peak age in both sexes is around 30 years old, and it can occur in any race and location in the world (SANT'ANA; SIQUEIRA, 2022).

The EULAR/ACR criteria (2019) are used to confirm the diagnosis, which is determined by the positivity of the antinuclear factor (ANF) greater than or equal to 1:80 simultaneously with the sum of 10 or more points according to the clinical and laboratory domains in the table. These domains are divided into: constitutional, cutaneous, articular, neurological, hematological, renal, serous, antiphospholipid antibodies, complement, highly specific antibodies (SANT'ANA; SIQUEIRA, 2022).

After diagnosis, the pathology can still be classified using various tools to define the inflammatory activity of the disease, such as ECLAM (*European Consensus Lupus Activity Measurement*), LAI (*Lupus Activity Index*) and SLEDAI (*Systemic Lupus Erythematosus Disease Activity Index*). These questionnaires are easy to reproduce and correlate well with each other to identify the degree of SLE activity (VERA GOLDER, et al., 2024).

In Brazil, the SLEDAI has been the most widely used for follow-up. It includes clinical and laboratory parameters in its assessment and has shown good results. This evaluation measure consists of a questionnaire that takes into account the last ten days of disease activity, which is classified according to the score obtained, being segmented into inactive (0 points), mild activity (1-5 points; shows that the disease activity index is weak, with minimal symptoms such as blood count and/or urinary changes or absent), moderate activity (6-10 points; suggests that there may be an increase in symptoms and inflammation, with alterations in blood count, urination and others such as arthritis and myositis), high activity (11-19 points; shows a significant presence of inflammation, with the same alterations already mentioned, plus vasculitis, stroke, lupus headache, neuropathy in cranial nerves), and very high activity (20 or more points; with the clinical picture of the other stages and associated with numerous other complications). In this sense, the SLEDAI is fundamental for the assessment, monitoring and treatment of patients with SLE, as it provides objective and standardized information that aids clinical decision-making (SOELISTYONINGSIH, et al., 2024).

When it comes to therapy, it's worth remembering that the approach is individualized and varies according to the organs and systems affected. Non-pharmacological measures are essential, including the use of photoprotection, lifestyle changes, adopting a balanced diet, psychological support and regular physical activity. These measures, combined with pharmacological measures, help to improve the clinical picture and reduce morbidity and mortality (KINGSMORE; ZENT; LIPSKY, 2024).

Pharmacological therapy, regardless of the organ or system affected, is prescribed through the continuous use of antimalarials, such as chloroquine diphosphate or hydroxychloroquine sulphate. These drugs are indicated to control the activity and prevent *flare-ups* of the disease, in order to avoid the chronic use of corticosteroids, which in the long term cau-

se problems such as osteoporosis, atherosclerosis and susceptibility to infections, among others. In acute crises, their use is unavoidable, and they are the first choice to avoid serious clinical outcomes. Later, when the crisis is in remission, the medication is gradually withdrawn and the use of antimalarials persists (ARINGER; YAZDANY, 2024). In refractory cases, immunosuppressive and/or immunomodulatory agents may be indicated, such as mycophenolate mofetil or sodium, cyclophosphamide, dapsone and thalidomide (KINGSMORE; ZENT; LIPSKY, 2024).

In addition, the literature points to studies that correlate SLE as a trigger for hematological changes, including anemia (BISWAS; AGGARWAL; GUPTA, 2018). These changes occur according to the inflammatory activity of the disease. Therefore, this study aims to relate the inflammatory activity of SLE through the use of SLEDAI with the changes present in the white and red blood count.

METHODOLOGY

This is a retrospective longitudinal study using a repeated measures design, carried out between June 2010 and February 2014, at the university general hospital (HGU), located in Cuiabá, capital of the state of Mato Grosso. The study population consisted of female patients diagnosed with SLE who were already undergoing treatment and were followed up between 06/2010 and 02/2014.

The patients lived in Cuiabá, were aged 18 or over, used the rheumatology outpatient clinic at the HGU and were diagnosed with SLE (ICD 10 M32), according to the ACR criteria. They were followed up during three consecutive clinical assessments. The exclusion criteria for the study were domicile outside Cuiabá and if their records of disease activity were incomplete.

This study was approved by the research ethics committee of HGU, University of Cuiabá, under registration No. 081/UNIC, Protocol 2010-062. All participants gave their informed consent. Disease activity was recorded at each visit using the systemic lupus erythematosus disease activity index (SELENA-SLEDAI).

The data selected is the relationship between the inflammatory activity of SLE by SELENA-SLEDAI simultaneously with the values found in the red and white blood count. These data were associated using Pearson's correlation, a descriptive statistical method that uses the "product-moment correlation coefficient" or "Pearson's p" to quantify two variables on a metric scale. It is a dimensionless measure and assesses the intensity of the relationship between the variables being analyzed.

RESULTS

There was a significant association between SLEDAI and hematocrit and MCV, which is exemplified by the negative values in Table 01, in which, when the inflammatory activity of SLE increases, there is an inversely proportional correlation with a decrease in the components of the red series: hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC).

The figurative elements of the blood count change together, so it's clear that the greater the degree of inflammation in SLE, the greater the alterations. In this particular analysis, the presence of anemia was evident in the patients, identified by an insufficient amount of hemoglobin. By classifying it according to its morphology, we can define it as microcytic and hypochromic, i.e. red blood cells with a reduction in size and a reduction in color, respectively

	SLEDAI	Red blood cells	Hemoglobin	Hematocrit	VCM	HCM	CHCM
SLEDAI	1	1					
Red blood cells	-0,093	0,614(**)					
Hemoglobin	-0,257	0,680(**)	1				
Hematocrit	-0,291(*)	-0,261	0,981(**)	1			
VCM	-0,307(*)	-0,183	0,573(**)	0,524(**)	1		
HCM	-0,264	0,056	0,656(**)	0,573(**)	0,972(**)	1	
CHCM	-0,020		0,673(**)	0,522(**)	0,599(**)	0,764(**)	1

Table 1 - Pearson's correlation between the SLEDAI and the red series in patients aged 18 or over at the rheumatology outpatient clinic of the university general hospital diagnosed with systemic lupus erythematosus from 2010-2014.

* p-value less than 0.05/ *p-value* < 0.05

** p-value less than 0.01/ *p-value* < 0.01

	SLEDAI	Leukocytes	Segmented	Neutrophils	Eosinophils	Basophils	Lymphocytes	Monocytes
SLEDAI	1							
Leukocytes	-0,068	1						
Segmented	0,085	0,353(*)	1					
Neutrophils	0,200	-0,090	0,503(**)	1				
Eosinophils	0,041	-0,240	-0,423(**)	-0,121	1			
Basophils	-0,144	0,387(**)	0,299(*)	-0,673(**)	-0,218	1		
Lymphocytes	-0,111	-0,293(*)	-0,966(**)	-0,371(**)	0,347(*)	-0,420(**)	1	
Monocytes	0,130	-0,561(**)	-0,697(**)	-0,178	0,120	-0,400(**)	0,593(**)	1

Table 2 - Pearson's correlation between the SLEDAI and the white series in patients aged 18 or over at the rheumatology outpatient clinic of a general hospital diagnosed with systemic lupus erythematosus from 2010-2014.

* p-value less than 0.05/ *p-value* < 0.05

** p-value less than 0.01/ *p-value* < 0.01

The relationship between the SLEDAI and the leukogram shows in Table 02 that there is leukopenia, basopenia and lymphopenia in proportion to the increase in inflammatory activity, demonstrating a significant drop in immune defense cells. This pattern is expected as the immune system causes aggression in the body itself, and its intensity will depend on the inflammatory activity, clinical manifestations and/or organs affected during the course of SLE.

In this sense, there is an inversely proportional relationship between some components of the leukogram: leukocytes with lymphocytes, neutrophils and monocytes; segmented leukocytes with lymphocytes, monocytes and eosinophils; neutrophils with basophils, lymphocytes and eosinophils; and basophils with lymphocytes and monocytes. This inverse association shows that when one increases, the other necessarily decreases, and the opposite situation can also occur depending on the patient's clinical condition.

DISCUSSION

The database of results shows some interesting factors, such as anemia, which, when compared with the study by NORIS-GARCÍA, et al, (2022), shows that this hematological alteration affects around 70% of patients diagnosed with SLE. In this context, it appears during the active phase of the disease, and is classified morphologically as normocytic anemia because it maintains a normal size pattern when compared to the pattern of the other red blood cells in the body, and normochromic because it main-

tains the normal color of the red blood cell. A classic example of anemia of chronic disease (BISWAS; AGGARWAL; GUPTA, V, 2018).

In addition, as shown in the current study, the morphological alteration can be explained by iron deficiency anemia, due to nutritional deficiencies caused by gastrointestinal malabsorption of nutrients and minerals, especially iron. This may be justified by the chronic use of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids and immunobiologicals in an attempt to reduce the activity and maintain remission of the disease (MORENO-TORRE, et al, 2022).

In addition to the CBC, it is necessary to assess iron reserves by means of serum iron, ferritin, transferrin and direct *Coombs*, since it can change according to the patient's clinical condition, the underlying etiology and the use of medication, in other words, anemia can occur that is different from the chronic disease pattern, such as iron deficiency, hemolytic, among others (BISWAS; AGGARWAL; GUPTA, 2018).

Among the causes of anemia, there is a complication at the bone marrow level, with cellular hypoproliferation due to a reduction in erythropoietin synthesis, showing that the initial problem is a renal impairment. There are also other phenomena, such as the self-destruction of erythrocytes due to the action of autoantibodies directed at cell surface antigens, generating autoimmune hemolysis, as well as other reasons such as blood loss and iron malabsorption (CHO, et al, 2022).

Among the other findings, leukopenia, basopenia and eosinopenia are mainly related to the autoimmune involvement of autoantibodies in the body, i.e. the immune system does not recognize the body's own cells, so this lack of cell recognition as non-constituents will lead to a drop in these white series cells and can be triggered by drugs, medullary suppression or hypersplenism (JÁTIVA, et al, 2024). This alteration occurs in approximately 50% of cases and, like red series alterations, has a strong relationship with kidney lesions and antibodies, especially anti-Sm (Smith antibody), due to its specificity for SLE (ABHIJIT; BIDYUT; ADITYA, 2024).

The leukocyte alterations predispose the individual to opportunistic infections, since the defense cells are reduced and leukopenia (leukocytes < 4000/mm^3, on two or more occasions) is one of the most relevant in terms of analysis. In addition to this susceptibility to infections, these changes result from deregulation in the cytokine network, T lymphocytes and the action of autoantibodies, all of which remodel the erythropoiesis process in the bone marrow (CIURTIN, et al, 2024), justifying this association between the inflammatory activity of SLE and these changes in the blood count.

CONCLUSION

The database shows that anemia is a common clinical manifestation in SLE, affecting around 70% of patients. It is classified morphologically as normocytic and normochromic, and is often associated with alterations in iron reserves (microcytic and hypochromic anemia), the form of presentation evident in the results of this study. It is also worth remembering that SLE can also cause leukopenia, basopenia and eosinopenia, increasing susceptibility to opportunistic infections due to the reduction in defense cells. These hematological changes are closely linked to the inflammatory activity of the disease and the action of autoantibodies.

Therefore, the treatment and follow-up of patients with SLE must take into account these complex interactions between the disease and the hematological system. Further research is needed to follow up patients for longer periods, as in this study, but with a more significant number (N) to analyze and correlate other hematological alterations.

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