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Original Article

Comparison of Clinical Features, Hematological Indices and Disease Activity between Early-Onset and Late-Onset Patients with Systemic Lupus Erythematosus

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Abstract

Background: Systemic lupus erythematosus (SLE) is an autoimmune chronic disease that may impact several organs. This research aimed to assess and evaluate the clinical symptoms, hematological parameters, and disease activity in SLE patients with early and late onset. Hematological indicators like neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and mean platelet volume (MPV) were also examined in order to determine how they relate to the severity and clinical manifestation of SLE.

Methods: One hundred patients in this cross-sectional study were chosen based on their compliance with the 2019 SLE criteria set by the European League Against Rheumatism and the American College of Rheumatology.Two equal groups of patients were formed: Early-onset SLE is in Group A, and late-onset SLE is in Group B.

Results: Malar rash, lymph node, arthritis and headache were substantially higher in group A than B ($P<0.05$). Compared to group A, group B had substantially greater cases of serositis and pleural effusion ($P<0.05$). Psychosis, thrombocytopenia bleeding tendency, previous coronary events and peripheral vascular events were insignificantly different between both groups. Group B had a much greater rate of anaemia manifestation compared to group A ($P<0.05$). NLR and PLR were significantly higher in group B than A ($P<0.05$). MPV, SLE activity index, proteinuria were insignificantly different between both groups.

Conclusions: Groups A (early onset SLE) and B (late onset SLE) showed different clinical characteristics. Group B (late onset SLE) showed distinct disease manifestations, including more serositis, pleural effusion, and anemia, suggesting that late-onset SLE may have unique features. Group A(early onset SLE) had more cases of malar rash, lymphadenopathy, arthritis, and headache. Additionally, group B(late onset SLE), had higher NLR and PLR, indicating increased systemic inflammation. Proteinuria, SLE activity index, and MPV did not vary significantly.

Keywords: Clinical Features, Disease Activity, Early-Onset, Hematological Indices, Late-Onset, Lupus Erythematosus

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease that affects several systems and organs. [1] Compared to men, women who are fertile are more likely to get SLE. [2] Although the underlying causes and mechanisms of SLE are not entirely clear, the loss of immune tolerance due to genetic factors and environmental exposures is widely believed to be a central factor in the disease's development. [3]

Autoantibody synthesis, prolonged inflammation, immune complex accumulation, and aberrant complement system activation are the key hallmarks of SLE, which typically results in numerous organ damage and a variety of clinical symptoms. [4]

Studies indicate that patients with late-onset SLE (those diagnosed after the age of fifty) usually exhibit symptoms that start more gradually and are not as severe. However, their long-term prognosis and death rate are often poorer and higher than those of people with SLE that begins before age 50. [5]

The use of hematological indices for assessing Disease activity in some autoimmune conditions, like rheumatoid arthritis and SLE, received more attention. [6]

Mean platelet volume (MPV) is the average platelets size found in circulation. [7] It is considered a marker of platelet activation and is often related to various inflammatory diseases.In the case of decreased platelet production, younger platelets are produced larger and more active, resulting in a coclusion that the size and count of platelets are inversely related. [8] Research suggests that myocardial infarction and cerebrovascular disease are associated with elevated MPV levels, while rheumatoid arthritis, ankylosing spondylitis, and ulcerative colitis are associated with decreased MPV levels throughout their active phases. [9]

One well-known indicator of inflammation that is determined by standard blood testing is the platelet-to-lymphocyte ratio (PLR). There is evidence that it is linked to disease activity and prognosis in several inflammatory diseases, such as cancer, sepsis, and autoimmune disorders like SLE. [10] PLR is calculated by dividing the total platelet count by the total lymphocyte count. [11]

The neutrophil-to-lymphocyte ratio (NLR) in peripheral blood is well-documented for its connection to inflammatory responses and its role in reflecting the inflammatory state of multiple diseases. [12]

Studies revealed a strong relationship between NLR and conditions such as axial spondyloarthritis (axSpA), Behçet's disease (BD), and rheumatoid arthritis (RA). [6]

Comparing the clinical features, hematological markers, and disease activity of patients with early versus late onset SLE was the aim of this study. Additionally, the association between hematological indices (MPV, PLR, and NLR) and SLE symptoms and the activity of disease was examined.

Patients and Methods:

This cross-sectional study included one hundred patients who satisfied the 2019 SLE diagnostic criteria set by the European League Against Rheumatism and the American College of Rheumatology. [13] On HEp-2 cells, the existence of antinuclear antibodies (ANA) was verified at a titer of > 1:80. If ANA is absent, SLE cannot be diagnosed. If ANA is present, the additive criteria should then be applied.

After The study received approval by the Sohag University Hospitals' Ethical Committee in Sohag, Egypt, patients or their families gave their informed written consent to take part.

Patients with cancer, pregnancy, other autoimmune illnesses, infections, or other long-term inflammatory diseases at the time of diagnosis, as well as those who had received immunosuppressive and glucocorticoid therapy, were excluded.

The patients were split into two equal groups: Group A, which included early-onset SLE, and Group B, which included late-onset SLE.

Clinical assessments were conducted on all patients, including a review of Alopecia, Raynaud's phenomenon, deep vein thrombosis history, Cutaneous vasculitis, fever, lupus-related

kidney inflammation (lupus nephritis), joint inflammation (arthritis), muscle inflammation (myositis), secondary antiphospholipid syndrome, inflammation of the serous membranes (serositis), pleural effusion , malar rash, discoid rash , photosensitivity, and ulcers in the mucous membranes or mouth , renal and hematological manifestations, thrombocytopenia, anemia, hypertension, diabetes mellitus, and prior coronary or peripheral vascular events were all reviewed as part of the clinical evaluations for each patient. A complete blood count with differential WBC count, ANA tests, serum creatinine, anti-dsDNA, anti-Sm, C3 and C4 complement levels, and, if required, anti-phospholipid markers were among the laboratory tests.

The SLEDAI score in this study was calculated using reliable laboratory and clinical finding. Disease activity was categorized as follows: The SLEDAI categorizes lupus activity into five levels: : no activity (0), high (11–19), extremely high (20), moderate (6–10), and mild (1–5). [14]

Statistical analysis

SPSS version 26 (IBM Inc., Chicago, IL, USA) was employed to analyze the data. To compare the two groups' quantitative data, an unpaired Student's t-test was employed. Mean and standard deviation were used to display the data. When applicable, we used Chi-square or Fisher's exact tests to examine the proportion and frequency of the qualitative variables. The two-tailed P value was considered statistically significant when it was less than 0.05.

Results

The two groups varied substantially in terms of age (P<0.05). Group A had much greater rates of malar rash, lymph node, arthritis, and headache (P<0.05). Group B had a substantial increase in serositis and pleural effusion (P<0.05). Sex, comorbidities, Discoid rash, photosensitivity, oral ulcer, alopecia, Raynaud's, History 0f DVT, cutaneous vasculitis, fever, myositis, secondary antiphospholipid, renal symptoms and seizer were insignificantly different between both groups. **Table 1**

Table 1: Demographic characteristics and comorbid conditions of the studied groups.

		Group A (n=50)	Group B (n=50)	P
Age (years)		26.66±6.14	56.16±8.77	**<0.001***
Sex	**Male**	1(2.0%)	0(0.0%)	1
	Female	49(98.0%)	50(100.0%)	
Comorbidities	**DM**	0(0.0%)	0(0.0%)	---
	HTN	8(16.0%)	11(22.0%)	0.444
Clinical manifestation	**Malar rash**	18(36.0%)	7(14.0%)	**0.011***
	Discoid rash	18(36.0%)	20(40.0%)	0.680
	Photosensitivity	8(16.0%)	9(18.0%)	0.790
	Oral ulcer	17(34.0%)	10(20.0%)	0.115
	Alopecia	42(84.0%)	42(84.0%)	1
	Raynaud's	9(18.0%)	8(16.0%)	0.790
	H\O of DVT	4(8.0%)	4(8.0%)	1
	Cutaneous vasculitis	1(2.0%)	0(0.0%)	1
	Fever	34(68.0%)	39(78.0%)	0.260
	Lymph node	34(68.0%)	24(48.0%)	**0.043***
	Arthritis	33(66.0%)	20(40.0%)	**0.009***
	Myositis	24(48.0%)	23(46.0%)	0.841
	Secondary antiphospholipid	4(8.0%)	12(24.0%)	0.053
	Serositis	7(14.0%)	18(36.0%)	**0.011***
	Pleural effusion	5(10.0%)	13(26.0%)	**0.037***
	Renal symptom	24(48.0%)	23(46.0%)	0.841
	Headache	39(78.0%)	28(56.0%)	**0.019***
	Seizere	1(2.0%)	4(8.0%)	0.362

Data is presented as mean ± SD or frequency. * Significant P value < 0.05. DM: Diabetes mellitus, HTN: Hypertension, DM: Diabetes mellitus, DVT: Deep venous thrombosis, H\O: History of.

Psychosis, thrombocytopenia bleeding tendency, previous coronary events and peripheral vascular events were insignificantly different between both groups. Group B had a much greater anaemic manifestation (P<0.05). **Table 2**

Table 2: Continue clinical manifestations of the studied groups

	Group A (n=50)	Group B (n=50)	P
Psychosis	2(4.0%)	1(2.0%)	1
DCL	0(0.0%)	0(0.0%)	---
Anaemic manifestation	15(30.0%)	25(50.0%)	**0.041***
Thrombocytopenia bleeding tendency	9(18.0%)	12(24.0%)	0.461
Previous coronary event	2(4.0%)	0(0.0%)	0.495
Peripheral vascular event	2(4.0%)	8(16.0%)	0.092

Data is presented as frequency (%). * Significant P value < 0.05. DCL: Disturbed conscious level.

Group B had substantially higher NLR and PLR compared to group A (P<0.05). MPV, SLE activity index, proteinuria were insignificantly different between both groups. **Table 3**

Table 3: NLR, PLR, MPV, SLE activity index, proteinuria of the studied groups

	Group A (n=50)	Group B (n=50)	P
NLR	2.49±1.93	5.14±6.55	**0.008***
PLR	183.29±156.46	296.47±308.6	**0.023***
MPV (Fl)	8.92±1.3	9.2±1.15	0.272
SLE activity index	20.02±5.57	18.96±4.26	0.288
Proteinuria	43(86.0%)	35(70.0%)	0.053

Data is presented as mean ± SD or frequency (%). * Significant P value < 0.05. NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, MPV: Mean platelet volume, SLE: Systemic lupus erythematosus.

Discussion

Multiple organs may be affected by SLE, a chronic autoimmune disease that causes a broad variety of symptoms in both the lab and the clinic. [15]

Our investigation did not find a substantial difference in the prevalence of hypertension (HTN) between the two groups. Additionally, no patients in either group had diabetes mellitus (DM).

In contrast to our study the findings by Mongkolchaiarunya et al. [16] observed that late-onset SLE patients were more likely to have HTN and DM. These differences could be attributed to variations in study populations or sample sizes.

Clinical features like Deep vein thrombosis (DVT) history, cutaneous vasculitis, discoid rash, photosensitivity, mouth ulcers, alopecia, Raynaud's phenomenon, fever, myositis, subsequent antiphospholipid syndrome, renal symptoms, and seizures did not significantly differ between early and late onset SLE.This was like Boddaert et al. [17] demonstrated that hematologic, mucocutaneous, and articular involvements were present in both early- and late-onset SLE patients, with serositis being more prevalent in the latter group.

Similarly, Sousa et al. [18] our research showed no discernible variations in antiphospholipid syndrome between early-onset and late-onset SLE. However, Choi et al. [19] found that adult-onset SLE was more likely to have antiphospholipid symptoms.

Consistent with what Xu et al. [20] found, we failed to detect a difference in renal affection between SLEs that manifested early rather than late. However, Choi et al. [19] revealed that proteinuria was much more common in SLE with an early onset.

This investigation found no significant changes in either nephropathy or photosensitivity between the two groups, Which differs from the results of Medlin Jl et al. [14], who found that both diseases were less common in late-onset SLE.

In line with previous research, the present study did not find any significant differences in the SLE Disease Activity Index between patients with early and late onset SLE. This finding is in support of the findings of Mongkolchaiarunya et al. [16], who also did not find any notable differences in clinical features or disease activity, although the late-onset group did have slightly more renal manifestations.

In this study, malar rash, lymphadenopathy, arthritis, and headache were significantly prevelant in early-onset group , while serositis and pleural effusion were more in late-onset SLE. Additionally, anaemic manifestations were significantly higher in late-onset one , and no cases of DCL were reported in either group. Our

findings of higher arthritis in early-onset group of SLE also correspond with that of Choi et al. [19] observed more musculoskeletal manifestations in adult-onset SLE.

Among the SLE subtypes studied here, early-onset SLE was substantially associated with a greater prevalence of malar rash., which was in agreement with Cildag et al. [21] In contrast to our study, El Bakry et al. [22] found that musculoskeletal symptoms were significantly higher in late-onset SLE.

According to this study, there were no documented cases of DCL in either group, and pleural effusion and serositis were more frequently linked to late-onset SLE. Additionally, late-onset SLE was more likely to exhibit anemic symptoms. According to Boddaert et al. [17], both early-onset and late-onset SLE affect the blood, however serositis is more common in the latter group.

Patients in late-onset group showed considerably higher NLRs and PLRs in this research when compared to early-onset one. These outcomes are consistent with El-Said et al., [23] who proposed that PLR could be a significant biomarker for both diagnosing SLE and predicting its activity.

There was no considerable difference in MPV and SLEDAI between the groups with early-onset and late-onset SLE, indicating that the disease activity was similar in both groups. However, a substantial positive correlation between MPV and SLEDAI was discovered by Kavitha [24] indicating that MPV may be a more important indicator of disease severity in some populations.

There was no considerable difference between patients with early-onset and late-onset SLE in terms of proteinuria. However,El Bakry et al. [22] found a notable difference, with the late-onset group showing more severe renal issues.
A limitation of the study was the small sample size and its single-location setting. We advise conducting more research in other locations with large sample sizes in order to compare results and provide more meaningful outcomes.

Conclusions

Clinical differences were found between groups A (early onset SLE) and B (late onset SLE). Group B (late onset SLE), being older, showed distinct disease manifestations, including more serositis, pleural effusion, and anemia, suggesting that late-onset SLE may have unique features. Group A (early onset SLE), being younger, had more cases of malar rash, lymphadenopathy, arthritis, and headache. Additionally, group B (late onset SLE) had higher NLR and PLR, indicating increased systemic inflammation. No significant differences were found in MPV, SLE activity index, or proteinuria. These findings highlight the need for age-based approaches to managing SLE.

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