



Systemic Lupus Erythematosus in Elderly Algerian Population

Naima Rania Belmokhtar^{1*}, Khalida Zemri¹, Khedoudja Kanoun¹, Harir Noria¹, Bachaoui B. M. Bouchra², Sid Tadj Hebri³ and Nadji Zouaoui³

¹Molecular Microbiology, Proteomics and Health Laboratory, Faculty of Natural and Life Sciences, Djillali Liabès University of Sidi Bel Abbés, Algeria

²Department of Internal Medicine-Diabetes, Etablissement Hospitalier Universitaire d'Oran 1 November 1954, Oran, Algeria

³Department Internal Medicine, University Hospital Centre CHU Dr Hassani Abdelkader, Sidi Bel Abbes, Algeria

*Corresponding author: Molecular Microbiology, Proteomics and Health Laboratory, Faculty of Natural and Life Sciences, Djillali Liabès University of Sidi Bel Abbés, Algeria. Email: avril_lavignerockstar@hotmail.fr

Received 2021 January 27; Revised 2021 April 19; Accepted 2021 April 28.

Abstract

Background: Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease, primarily affecting young women of childbearing age. SLE is rare in the elderly and represents clinico-biological characteristics in this age group different from those of young patients.

Objectives: To determine the clinical-biological and prognostic specificities of 12 cases of SLE emerged after the age of 50 years and compare them with some cases of early-onset SLE.

Methods: On a total of 203 SLE patients, 12 cases aged of 50 years and above were examined. All SLE patients were who had been diagnosed according to the ACR and SLICC criteria and followed up during 2006 - 2019 in two western Algeria hospitals.

Results: Twelve patients with late SLE were diagnosed during the research period. The mean age of attack in this age group was 59.17 ± 11.10 years, and the mean age of clinical diagnosis was 67.67 ± 10.95 years. Among the concerned cases, ten patients (83.3%) were postmenopausal women, and two participants were men (16.7%) with an F/M gender ratio of 5 : 1. The mean duration of follow-up was 8.5 ± 4.33 years. The most frequent revealing clinico-serological characteristics were dermatological, articular, hematological, and pulmonary damage (58.3%, 91.7%, 58.3%, and 33.3% respectively), the positivity of anti-dsDNA antibodies (75%), anti-Sm/anti-SSA (41.7%), and hypocomplementemia (25%). Moreover, renal and neuropsychiatric damage was rare after the age of 50 years. The leading cause of death was stroke, with a significantly higher mortality rate in the elderly group ($P < 0.001$).

Conclusions: SLE in the elderly is rare, its diagnosis may be delayed due to the insidious onset, and its low prevalence and similarity and comorbidity with other more common disorders make its diagnosis difficult, especially in this subgroup.

Keywords: Mortality, Late-Onset, Elderly, Systemic Lupus Erythematosus

1. Background

Systemic lupus erythematosus (SLE) is a polymorphic autoimmune disease that primarily affects young women (1, 2). Its highest incidence is reported in individuals aged 15 - 40 years (3). Lupus is rare and more insidious in the elderly than in younger patients. It is defined by its onset after the age of 50 years. The incidence of this disease is estimated to be 4 - 16% in most studies (1, 4-11).

Several studies have examined late-onset SLE, suggesting that the age of onset alters the clinical expression of the disease in terms of onset, clinical presentation, organ involvement pattern, and serological findings. In this regard, different modes of presentation, including arthritis and lung disease, have been described. The most consistent features in elderly patients have been the higher frequency of arthritis and the lower frequency of Raynaud's

disease, neuropsychiatric involvement, and severe kidney injury. Serologic abnormalities have also been reported to be different in elderly patients.

2. Objectives

The present study aimed to define the clinical, biological, and prognostic specificities of 12 cases of SLE emerged after the age of 50 years and compare these data with early-onset SLE cases as those described in the literature.

3. Methods

This retrospective multicenter study included consulting patients' files. We identified 12 patients with SLE at the age of 50 years and above (group A) from 2006 to 2019 in two Western Algeria hospitals: the University Hospital of

Oran (EHUO) and the University Hospital Abdelkader Hasani of Sidi Bel Abbes (CHU-SBA). We also included 191 patients with onset SLE at the age of 13 - 49 years (group B). In total, two hundred and three patients were included in our study. Group A encompassed postmenopausal women. Inclusion criteria were the presence of at least four criteria from the 1982 American college of rheumatology (ACR) SLE classification, as revised in 1997 (12, 13). The criteria approved by SLE and SLEDAI (lupus disease activity index) were used (14).

Late-onset SLE is defined by the age of first symptoms retrospectively attributable to SLE. The clinical-biological characteristics (at the initial phase and during the course) and immunological, therapeutic, and comorbidities features have also been described in this regard.

3.1. Statistics

We used the Statistical Package for the Social Sciences (SPSS 22.0 Inc, Chicago, IL, USA) for all conventional analyses. Means and standard deviations were calculated for the age of onset, age at diagnosis, duration between first symptoms and the disease, and follow-up duration. The Person chi-squared test with Fisher's correction was used to compare the numbers. In this study, the significance level was set as $P \leq 0.05$.

4. Results

We studied the clinical records of 203 patients with SLE (90.6% female and 9.4% male), with a F/M gender ratio of 9.86/1. The mean age of the disease onset was 29.47 ± 11.24 years. The mean duration of follow-up was 12.7 ± 9.18 years.

In 12 patients, the age of disease onset was 50 years and above (≥ 50 years). This group of patients (A) was compared with 191 patients in group B (disease onset, 13 to 49 years). The mean age of the disease onset in group A was 59.17 ± 11.10 years (range: 50 and 89 years), and the mean age of clinical diagnosis was 67.67 ± 10.95 years. Ten patients (83.3%) were postmenopausal women, and two participants were men (16.7%). The gender ratio of female to male was 5 to 1 and 10 to 1 in groups A and B, respectively. The mean duration of follow-up was 8.5 ± 4.33 years in group A and 13.02 ± 9.34 in group B. (Table 1).

Table 2 presents the frequency of initial manifestations for the two age groups. The most frequent clinical manifestations of group A were arthritis (91.7%), malar rash (58.3%), photosensitivity (41.7%), Hematological involvement (58.3%), and lupus pneumonia (33.3%). Lupus nephritis was found in a single patient (8.3%) in group A and 50 patients (26.2%) in group B. Moreover, the mortality rate was significantly higher in the younger group than in the older group ($P = 0.024$).

Table 3 lists the serological results as a function of age. Using the SLEDAI criteria, we compared the severity of SLE between the two groups. In this table, the ACR criteria numbers are also included. In group A, the serological analysis showed the positivity of anti-dsDNA antibodies at 75 and 41.7% for each of anti-Sm anti-SSA, and 25% hypocomplementemia. No significant difference was noticed regarding the incidence of autoantibodies (dsDNA, Ro, La, Sm, and RNP).

Early-onset patients (group B) showed a significantly higher prevalence of neutropenia ($P = 0.053$) than late-onset patients (group A).

The presence of other pathologies associated with lupus disease has been noticed in groups A, and B as 41.7% vs. 15.2% of the participants had arterial hypertension (hypertension), 16.7% vs. 4.2% of the cases suffered from Gougerot Sjogren syndrome (SGS), and 16.7% vs. 6.8% of the participants had rheumatoid arthritis (RA). Diabetes was observed in only one case (8.3%) and in 12.6% of the patients in group B. Other autoimmune pathologies, such as dermatomyositis (DPM), psoriasis, Hashimoto's thyroiditis, were observed in the two groups (75% vs. 32.5%). A significant correlation between the presence of arterial hypertension was found between the two groups (41.7% vs. 15.2%, $P = 0.056$).

Table 4 indicates that cerebrovascular accident (stroke) as the leading cause of death in both groups. A significant difference was found in the incidence of CVA, renal failure, and septic shock with $P = 0.003$, $P = 0.018$, and $P = 0.059$, respectively.

5. Discussion

Late-onset SLE represents a specific disease subgroup, as most cases are noted in postmenopausal women (15). It begins at the age of 50 - 65 years old and above (4, 16, 17). Late SLE is rare as it affects only 12 - 18% of the population (4, 18, 19).

Out of 203 SLE patients, twelve patients (9.4%) of developed the disease after the age of 50 years. This frequency is similar to that reported in some other studies (7 - 18%) (4, 7, 20, 21). A female predominance in the group of the elderly was noted in our cases as well as other cases reported in the literature (19, 21, 22). However, some reports have suggested that the female predominance is not so marked in the elderly (7, 20, 23). In general, other studies have reported a significantly higher incidence of male lupus in this age group (1, 7, 24-26). The gender ratio of women to men declined in the elderly group, as revealed in previous reports. In our study, the F/M ratio in group A was similar to the ratio reported in other studies (19, 27). However, it

Table 1. Demographics Data of SLE Patients by the Age of Onset^a

	Group A (≥ 50 y, n = 12)	Group B (< 50 y, n = 191)	P-Value
Gender			0.312
Male	2 (16.7)	17 (8.9)	
Female	10 (83.3)	174 (91.1)	
Age at onset (y)	59.17 \pm 11.10	27.61 \pm 8.25	< 0.001
Age at diagnosis (y)	67.67 \pm 10.95	40.75 \pm 12.45	0.044
Duration from onset to diagnosis (y)	8.5 \pm 4.33	13.02 \pm 9.34	0.868

^a Values are expressed as No. (%) or mean \pm SD.

Table 2. Clinical Data of SLE Patients by the Age of Onset^a

	Group A (≥ 50 y, n = 12)	Group B (< 50 y, n = 191)	P Value
General signs			
Fever	1 (8.3)	20 (10.5)	0.793
Asthenia	3 (25)	80 (41.9)	0.366
Weight loss	1 (8.3)	37 (19.4)	0.471
Anorexia	1 (8.3)	18 (9.4)	1.000
Dermatological disorders	7 (58.3)	138 (72.3)	0.329
Malar rash	5 (41.7)	106 (55.5)	0.384
Photosensitivity	5 (41.7)	78 (40.8)	1.000
Oral ulcer	4 (33.3)	30 (15.7)	0.121
Alopecia	2 (16.7)	39 (20.4)	1.000
Arthritis	11 (91.7)	143 (74.9)	0.300
Pericarditis	1 (8.3)	12 (6.3)	0.932
Renal involvement	1 (8.3)	50 (26.2)	0.302
Lupus pneumonitis	4 (33.3)	64 (33.5)	0.820
Neuropsychiatric	0	25 (13.1)	0.317
Haematological disorder	7 (58.3)	139 (72.8)	0.351
Raynaud's syndrome	1 (8.3)	51 (26.7)	0.318
Sjogren's syndrome	2 (16.7)	8 (4.2)	0.142
APLS	1 (8.3)	20 (10.5)	0.880
Gastrointestinal damage	0	5 (2.6)	0.694
Mortality	6 (50)	5 (2.6)	< 0.001

Abbreviation: APLS, antiphospholipid syndrome.

^a Data are presented as No. (%).

was lower than that of the younger group, 10.23 : 1 (group B).

Regarding the length of time from onset to diagnosis, the younger group has a significantly longer duration than the older group. (8.5 vs. 13.02 years). On the other hand, many previous reports demonstrated that this duration was longer in the older than in, the younger patients (19, 28, 29).

Numerous studies have suggested that patients with late-onset lupus differ from those with early-onset lupus in their clinical presentation, organ involvement pattern, and disease severity. Accordingly, different conclusions were drawn, possibly due to racial differences (4, 17).

The clinical course of late-onset SLE is considered milder. In patients with late SLE compared to patients with SLE at an earlier age, skin manifestations, nephritis,

Table 3. Biological Analysis of SLE Patients by the Age of Onset^a

	Group A (≥ 50 y, n = 12)	Group B (< 50 y, n = 191)	P Value ^b
Hematologic disorders	7 (58.3)	139 (72.8)	0.351
Hemolytic anemia	2 (16.7)	17 (8.9)	0.312
Leukopenia	2 (16.7)	42 (22)	1.000
Lymphopenia	2 (16.7)	63 (33)	0.345
Neutropenia	2 (16.7)	8 (4.2)	0.111
Thrombocytopenia	3 (25)	44 (23)	1.000
Antinuclear antibody	9 (75)	170 (89)	0.156
Anti-dsDNA antibody	9 (75)	117 (61.3)	0.541
Anti-Sm antibody	5 (41.7)	58 (30.4)	0.521
Anti-RNP antibody	3 (25)	38 (19.9)	0.711
Anti-SSA antibody	5 (41.7)	67 (35.1)	0.758
Anti-SSB antibody	2 (16.7)	30 (15.7)	1.000
APL	1 (8.3)	24 (12.6)	1.000
Anti-Histone	1 (8.3)	15 (7.9)	1.000
Anti-nucleosome	1 (8.3)	10 (5.2)	0.497
Hypocomplementemia	3 (25)	65 (34)	0.754
VDRL test	2 (16.7)	7 (3.7)	0.092

Abbreviations: dsDNA, double-stranded DNA; RNP, ribonucleoprotein; VDRL, Venereal Disease Research Laboratory.

^a Data are presented as No. (%) or mean \pm standard deviation.

^b P-value from chi-square test of Person with Fisher exact test.

Table 4. Death Causes of SLE Patients by the Age of Onset^a

	Group A (≥ 50 y, n = 12)	Group B (< 50 y, n = 191)	P-Value
Number of deaths	6 (50)	5 (2.6)	< 0.001
CVA	3 (25)	3 (1.6)	0.003
Renal failure	2 (16.7)	2 (1)	0.018
Septic shock	1 (8.3)	0 (0)	0.059

Abbreviation: CVA, cerebrovascular accident.

^a Data are presented as No. (%).

neuropsychiatric, and cardiac manifestations were less frequent (4, 19, 21, 30). In our study and many other studies, malaria erythema was also less common in older individuals with SLE (1, 6-9, 29, 31, 32). In contrast, photosensitivity is more frequent in the present study and Dimant et al.'s (5) study. Likewise, oral ulcerations are more frequent in this study and the study by Chen et al. (28). These differences can be justified by differences in sun exposure in different countries.

Regarding the late SLE cases, we observed a higher incidence of lung involvement and Sjögren's syndrome, similar to other studies (4, 19, 21, 30, 33). Likewise, arthritis was more common in the elderly than in younger patients. This finding was in contrast with some other studies (4, 19, 21,

30, 34, 35).

Similar to the present study, Madisson (19) reported the higher prevalence of cardiovascular complications in a group of 86 patients with late-onset SLE (8.3% vs. 6.3%). Regarding clinical characteristics, no significant difference was found between the two groups. as the same was also noticed for biological analyses, except neutropenia ($P = 0.053$) (Table 3). In contrast, Wilson et al. (30), Ballou et al. (20), and Chen et al. (28) found a significant difference between patients with late SLE and younger participants in terms of three immunological criteria (anti-dsDNA antibody, hypocomplementemia, and anti-RNP antibody). Likewise, hemolytic anemia has been more common in the elderly, as reported in three other recent stud-

ies (11, 31, 36). A higher positive level of anti-SSA and anti-SSB antibodies in the case of late SLE was noted in the present cases and several cases in the literature (21, 25, 34, 36, 37). Anti-Sm antibodies and anti-RNP were also found at a high level in the late SLE cases in the present study. In contrast, these antibodies are found at low frequency in other studies (1, 19, 25, 38). Our patients with late-onset lupus also have less frequent hypocomplementemia; however, this is not constant compared to younger patients (5, 16, 19, 20, 30, 34, 39), which is not surprising given the less severe manifestations of the disease. The same findings are also revealed in several other studies.

Concerning the disease severity, no significant difference was noticed between groups A and B. The patients with late SLE showed a high mortality rate ($P = 0.024$). This finding is consistent with those reported by Chen et al. ($P = 0.022$) (28) and some other researchers (8, 29, 38).

In both groups, stroke was the common cause of death and was mainly associated with the presence of high blood pressure (hypertension). Similarly, Bertoli et al. (38) reported cardiovascular pathologies as the leading cause of death in patients with late-onset SLE. In contrast, in their studies, Chen et al. (28) and Pu et al. (29) reported septic shock as the leading cause of death.

The small sample size of our late SLE patients was a limiting factor in the present study. Accordingly, large-scale studies are recommended to further examine the molecular physiopathology of this disease.

5.1. Conclusions

The low prevalence of late SLE and the presence of comorbidity with similar symptoms in the elderly patients make the diagnosis difficult. Accordingly, further attention to this patients group is needed to avoid diagnostic delays.

Acknowledgments

We would like to thank the patients for their participation and the staff at the Internal Medicine of the University Hospital of Oran (EHUO) and the University Hospital of Sidi-bel-Abbes (CHU-SBA) for their valuable support, guidance, and educational insight.

Footnotes

Authors' Contribution: Study concept and design: Naima Rania Belmokhtar; Khalida Zemri; Khedoudja Kanoun; Noria Harir; B. M. Bachaoui; Sid Tadj Hebri; Nadji Zouaoui. Data collection: Naima Rania Belmokhtar; Noria Harir; B. M. Bachaoui. Analysis and interpretation of data:

Naima Rania Belmokhtar; Noria Harir; B. M. Bachaoui; Sid Tadj Hebri, Nadji Zouaoui. Drafting of the manuscript: Naima Rania Belmokhtar; Khalida Zemri; Khedoudja Kanoun; Noria Harir; B. M. Bachaoui; Sid Tadj Hebri; Nadji Zouaoui. Critical revision of the manuscript for important intellectual content: Naima Rania Belmokhtar; Khalida Zemri; Khedoudja Kanoun; Noria Harir; B. M. Bachaoui; Sid Tadj Hebri; Nadji Zouaoui. Statistical analysis: Naima Rania Belmokhtar; Khalida Zemri; Noria Harir. Administrative, technical, and material support: Naima Rania Belmokhtar; Khalida, Noria Harir; B.M. Bachaoui; Sid Tadj Hebri; Nadji Zouaoui. Study supervision: Naima Rania Belmokhtar; Khalida Zemri; Khedoudja Kanoun; Noria Harir; B.M. Bachaoui; Sid Tadj Hebri; Nadji Zouaoui.

Conflict of Interests: The authors have declared no potential conflict of interests concerning the research, authorship, and/or publication of this article.

Data Reproducibility: It was not declared by the authors.

Ethical Approval: The local Ethics Committee of the University Hospital approved the present study.

Funding/Support: The authors received no financial support for this article's research, authorship, and/or publication.

References

1. Cervera R, Khamashta MA, Font J, Sebastiani GD, Gil A, Lavilla P, et al. Systemic lupus erythematosus: clinical and immunologic patterns of disease expression in a cohort of 1,000 patients. The European Working Party on Systemic Lupus Erythematosus. *Medicine (Baltimore)*. 1993;72(2):113-24. [PubMed: 8479324].
2. Dubois EL, Tuffanelli DL. Clinical Manifestations of Systemic Lupus Erythematosus. Computer Analysis of 520 Cases. *JAMA*. 1964;190:1104-11. doi: 10.1001/jama.1964.03070150014003. [PubMed: 14184513].
3. Hughes GR. Systemic lupus erythematosus. *Postgrad Med J*. 1988;64(753):517-21. doi: 10.1136/pgmj.64.753.517. [PubMed: 3074284]. [PubMed Central: PMC2428894].
4. Baker SB, Rovira JR, Campion EW, Mills JA. Late onset systemic lupus erythematosus. *Am. J. Med.* 1979;66(5):727-32. doi: 10.1016/0002-9343(79)91109-4.
5. Dimant J, Ginzler EM, Schlesinger M, Diamond HS, Kaplan D. Systemic lupus erythematosus in the older age group: computer analysis. *J Am Geriatr Soc*. 1979;27(2):58-61. doi: 10.1111/j.1532-5415.1979.tb03342.x. [PubMed: 762367].
6. Koh ET, Boey ML. Late onset lupus: a clinical and immunological study in a predominantly Chinese population. *J Rheumatol*. 1994;21(8):1463-7. [PubMed: 7983647].
7. Font J, Pallares L, Cervera R, Lopez-Soto A, Navarro M, Bosch X, et al. Systemic lupus erythematosus in the elderly: clinical and immunological characteristics. *Ann Rheum Dis*. 1991;50(10):702-5. doi: 10.1136/ard.50.10.702. [PubMed: 1958093]. [PubMed Central: PMC1004535].
8. Boddaert J, Huong DLT, Amoura Z, Wechsler B, Godeau P, Piette JC. Late-onset systemic lupus erythematosus: a personal series of 47 patients and pooled analysis of 714 cases in the literature. *Medicine (Baltimore)*. 2004;83(6):348-59. doi: 10.1097/01.md.0000147737.578617c. [PubMed: 15525847].

9. Lalani S, Pope J, de Leon F, Peschken C, Members of Ca NFOI. Clinical features and prognosis of late-onset systemic lupus erythematosus: results from the 1000 faces of lupus study. *J Rheumatol*. 2010;**37**(1):38-44. doi: [10.3899/jrheum.080957](https://doi.org/10.3899/jrheum.080957). [PubMed: [20008925](https://pubmed.ncbi.nlm.nih.gov/20008925/)].
10. Maamar M, Tazi Mezalek Z, Harmouche H, Ammouri W, Bachir H, Adnaoui M, et al. [Late-onset lupus: retrospective study of 25 cases]. *Rev. Med. Interne*. 2012;**33**(Supplement 1). French. doi: [10.1016/j.revmed.2012.03.263](https://doi.org/10.1016/j.revmed.2012.03.263).
11. Tomic-Lucic A, Petrovic R, Radak-Perovic M, Milovanovic D, Milovanovic J, Zivanovic S, et al. Late-onset systemic lupus erythematosus: clinical features, course, and prognosis. *Clin Rheumatol*. 2013;**32**(7):1053-8. doi: [10.1007/s10067-013-2238-y](https://doi.org/10.1007/s10067-013-2238-y). [PubMed: [23515605](https://pubmed.ncbi.nlm.nih.gov/23515605/)].
12. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum*. 1997;**40**(9):1725. doi: [10.1002/art.1780400928](https://doi.org/10.1002/art.1780400928). [PubMed: [9324032](https://pubmed.ncbi.nlm.nih.gov/9324032/)].
13. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum*. 1982;**25**(11):1271-7. doi: [10.1002/art.1780251101](https://doi.org/10.1002/art.1780251101). [PubMed: [7138600](https://pubmed.ncbi.nlm.nih.gov/7138600/)].
14. Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH. Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. *Arthritis Rheum*. 1992;**35**(6):630-40. doi: [10.1002/art.1780350606](https://doi.org/10.1002/art.1780350606). [PubMed: [1599520](https://pubmed.ncbi.nlm.nih.gov/1599520/)].
15. McCarty DJ, Manzi S, Medsger TA, Ramsey-Goldman R, LaPorte RE, Kwoh CK. Incidence of systemic lupus erythematosus. Race and gender differences. *Arthritis Rheum*. 1995;**38**(9):1260-70. doi: [10.1002/art.1780380914](https://doi.org/10.1002/art.1780380914). [PubMed: [7575721](https://pubmed.ncbi.nlm.nih.gov/7575721/)].
16. Formiga F, Moga I, Pac M, Mitjavila F, Rivera A, Pujol R. Mild presentation of systemic lupus erythematosus in elderly patients assessed by SLEDAI. SLE Disease Activity Index. *Lupus*. 1999;**8**(6):462-5. doi: [10.1177/096120339900800609](https://doi.org/10.1177/096120339900800609). [PubMed: [10483015](https://pubmed.ncbi.nlm.nih.gov/10483015/)].
17. Padovan M, Govoni M, Castellino G, Rizzo N, Fotinidi M, Trotta F. Late onset systemic lupus erythematosus: no substantial differences using different cut-off ages. *Rheumatol Int*. 2007;**27**(8):735-41. doi: [10.1007/s00296-006-0284-3](https://doi.org/10.1007/s00296-006-0284-3). [PubMed: [17195066](https://pubmed.ncbi.nlm.nih.gov/17195066/)].
18. Gladman DD, Urowitz MB. Systemic lupus erythematosus. Clinical features. *Rheumatol. Connective tissue disorders*. London, UK: Mosby; 1994. p. 2239-41.
19. Maddison PJ. Systemic lupus erythematosus in the elderly. *J Rheumatol Suppl*. 1987;**14**(Suppl 13):182-7.
20. Ballou SP, Khan MA, Kushner I. Clinical features of systemic lupus erythematosus: differences related to race and age of onset. *Arthritis Rheum*. 1982;**25**(1):55-60. doi: [10.1002/art.1780250109](https://doi.org/10.1002/art.1780250109). [PubMed: [6978135](https://pubmed.ncbi.nlm.nih.gov/6978135/)].
21. Catoggio LJ, Skinner RP, Smith G, Maddison PJ. Systemic lupus erythematosus in the elderly: clinical and serological characteristics. *J Rheumatol*. 1984;**11**(2):175-81. [PubMed: [6610051](https://pubmed.ncbi.nlm.nih.gov/6610051/)].
22. Domenech I, Aydintug O, Cervera R, Khamashta M, Jedryka-Goral A, Vianna JL, et al. Systemic lupus erythematosus in 50 year olds. *Postgrad Med J*. 1992;**68**(800):440-4. doi: [10.1136/pgmj.68.800.440](https://doi.org/10.1136/pgmj.68.800.440). [PubMed: [1437923](https://pubmed.ncbi.nlm.nih.gov/1437923/)]. [PubMed Central: [PMC2399336](https://pubmed.ncbi.nlm.nih.gov/PMC2399336/)].
23. Hochberg MC, Boyd RE, Ahearn JM, Arnett FC, Bias WB, Provost TT, et al. Systemic lupus erythematosus: a review of clinico-laboratory features and immunogenetic markers in 150 patients with emphasis on demographic subsets. *Medicine (Baltimore)*. 1985;**64**(5):285-95. [PubMed: [2412088](https://pubmed.ncbi.nlm.nih.gov/2412088/)].
24. Jacobsen S, Petersen J, Ullman S, Junker P, Voss A, Rasmussen JM, et al. A multicentre study of 513 Danish patients with systemic lupus erythematosus. I. Disease manifestations and analyses of clinical subsets. *Clin Rheumatol*. 1998;**17**(6):468-77. doi: [10.1007/BF01451282](https://doi.org/10.1007/BF01451282). [PubMed: [9890674](https://pubmed.ncbi.nlm.nih.gov/9890674/)].
25. Costallat LT, Coimbra AM. Systemic lupus erythematosus: clinical and laboratory aspects related to age at disease onset. *Clin Exp Rheumatol*. 1994;**12**(6):603-7. [PubMed: [7895393](https://pubmed.ncbi.nlm.nih.gov/7895393/)].
26. Hashimoto H, Tsuda H, Hirano T, Takasaki Y, Matsumoto T, Hirose S. Differences in clinical and immunological findings of systemic lupus erythematosus related to age. *J Rheumatol*. 1987;**14**(3):497-501. [PubMed: [3625631](https://pubmed.ncbi.nlm.nih.gov/3625631/)].
27. Voulgari PV, Katsimbri P, Alamanos Y, Drosos AA. Gender and age differences in systemic lupus erythematosus. A study of 489 Greek patients with a review of the literature. *Lupus*. 2002;**11**(11):722-9. doi: [10.1191/0961203302lu2530a](https://doi.org/10.1191/0961203302lu2530a). [PubMed: [12475002](https://pubmed.ncbi.nlm.nih.gov/12475002/)].
28. Chen TL, Wong C, Lee C, Loo JH, Lin M. Systemic Lupus Erythematosus in the Elderly. *Int J Gerontol*. 2009;**3**(2):108-13. doi: [10.1016/s1873-9598\(09\)70030-4](https://doi.org/10.1016/s1873-9598(09)70030-4).
29. Pu SJ, Luo SF, Wu YJ, Cheng HS, Ho HH. The clinical features and prognosis of lupus with disease onset at age 65 and older. *Lupus*. 2000;**9**(2):96-100. doi: [10.1191/096120300678828109](https://doi.org/10.1191/096120300678828109). [PubMed: [10787005](https://pubmed.ncbi.nlm.nih.gov/10787005/)].
30. Wilson HA, Hamilton ME, Spyker DA, Brunner CM, o'Brien WM, Davis J, et al. Age influences the clinical and serologic expression of systemic lupus erythematosus. *Arthritis Rheum*. 1981;**24**(10):1230-5. doi: [10.1002/art.1780241002](https://doi.org/10.1002/art.1780241002). [PubMed: [6975629](https://pubmed.ncbi.nlm.nih.gov/6975629/)].
31. Zulfiqar AA, Courtel T, Novella JL, Pennaforte JL. [Late-onset lupus in the elderly after 65 years: retrospective study of 18 cases]. *Geriatr Psychol Neuropsychiatr Vieil*. 2015;**13**(2):157-68. doi: [10.1684/pnv.2015.0541](https://doi.org/10.1684/pnv.2015.0541). [PubMed: [26103107](https://pubmed.ncbi.nlm.nih.gov/26103107/)].
32. Gaujard S, Broussole C, Cathebras P, Dupond JL, Massot C, Ninet J, et al. [Systemic lupus erythematosus with disease onset at 65 and older]. *Rev. Med. Interne*. 2003;**24**(5):288-94. French. doi: [10.1016/s0248-8663\(03\)00052-3](https://doi.org/10.1016/s0248-8663(03)00052-3).
33. Tuchyňová A, Rovenský J, Lukáč J. [Older systemic lupus erythematosus: a retrospective study]. *Čes Revmatol*. 1998;**6**(123-6). Slovak.
34. Ward MM, Polisson RP. A meta-analysis of the clinical manifestations of older-onset systemic lupus erythematosus. *Arthritis Rheum*. 1989;**32**(10):1226-32. doi: [10.1002/anr.1780321007](https://doi.org/10.1002/anr.1780321007). [PubMed: [2803325](https://pubmed.ncbi.nlm.nih.gov/2803325/)].
35. Rovenský J, Tuchyňová A. Systemic lupus erythematosus in the elderly. *Autoimmun Rev*. 2008;**7**(3):235-9. doi: [10.1016/j.autrev.2007.11.014](https://doi.org/10.1016/j.autrev.2007.11.014). [PubMed: [18190884](https://pubmed.ncbi.nlm.nih.gov/18190884/)].
36. Appenzeller S, Pereira DA, Costallat LT. Greater accrual damage in late-onset systemic lupus erythematosus: a long-term follow-up study. *Lupus*. 2008;**17**(11):1023-8. doi: [10.1177/0961203308089695](https://doi.org/10.1177/0961203308089695). [PubMed: [18852227](https://pubmed.ncbi.nlm.nih.gov/18852227/)].
37. Mak SK, Lam EK, Wong AK. Clinical profile of patients with late-onset SLE: not a benign subgroup. *Lupus*. 1998;**7**(1):23-8. doi: [10.1191/096120398678919723](https://doi.org/10.1191/096120398678919723). [PubMed: [9493145](https://pubmed.ncbi.nlm.nih.gov/9493145/)].
38. Bertoli AM, Alarcon GS, Calvo-Alen J, Fernandez M, Vila LM, Reveille JD, et al. Systemic lupus erythematosus in a multiethnic US cohort. XXXIII. Clinical [corrected] features, course, and outcome in patients with late-onset disease. *Arthritis Rheum*. 2006;**54**(5):1580-7. doi: [10.1002/art.21765](https://doi.org/10.1002/art.21765). [PubMed: [16645994](https://pubmed.ncbi.nlm.nih.gov/16645994/)].
39. Shaikh SK, Wang F. Late-onset systemic lupus erythematosus: clinical and immunological characteristics. *Med J Malaysia*. 1995;**50**(1):25-31. [PubMed: [7752972](https://pubmed.ncbi.nlm.nih.gov/7752972/)].