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Research Article

Comparison of Comorbid Diseases Between Early-Onset and Late- Onset Systemic Lupus Erythematosus; A Single Center Retrospective Experience

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Abstract

Aim: To examine the comorbidity profile of patients with systemic lupus erythematosus (SLE) and to evaluate differences in comorbidity burden between late-onset and early-onset SLE patients.

Material and Method: We retrospectively analyzed SLE patients who presented to the tertiary rheumatology clinic between February 2024 and February 2025. Patients were categorized by age at diagnosis into three groups: childhood-onset (<18 years), adult-onset (18–49 years), and late-onset (≥50 years). Comorbidities were systematically documented and compared across groups.

Results: 284 SLE patients were included, with a mean age at diagnosis of 37.2 (±11.2) years; 83.8% were female. Arterial hypertension was the most common comorbidity (23.9%). Of the patients, 27 (7.1%) had childhood-onset SLE, 176 (61.9%) had adult-onset, and 81 (28.5%) had late-onset SLE. Arterial hypertension (46.9% vs. 15.9% and 7.4%, p_1=0.004, p_2=0.0021) and osteoporosis (22.2% vs. 4.5% and 3.7%, p_1=0.014, p_2=0.032) were more common in the late-onset SLE. The childhood SLE had higher rate of autoimmune thyroid diseases (22.2%), although differences between groups were not statistically significant.

Conclusion: Comorbid conditions, such as arterial hypertension and osteoporosis are more prevalent in late-onset SLE patients. These comorbidities may complicate disease management and should be considered as part of a comprehensive treatment strategy to optimize outcomes in daily clinical practice.

Keywords: Systemic lupus erythematosus, comorbidity, late-onset systemic lupus erythematosus, arterial hypertension, osteoporosis

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease that can present at various ages and manifests with diverse clinical subphenotypes (1). Although high morbidity and mortality due to severe organ involvement at diagnosis or during the disease course remain significant concerns, outcomes have improved considerably over the past five decades with the increased use of immunosuppressive therapies (2). Despite these advances, the comorbidities in SLE continues to influence treatment decisions and therapeutic success (3,4).

In addition to conventional risk factors, persistent inflammation related to SLE and the adverse effects of medications—particularly glucocorticoids—may predispose patients to the development of comorbid conditions (5). These comorbidities are also associated with reduced quality of life and make disease activity more difficult to manage (6). Although comorbidity burden generally increases with age, it is noteworthy that childhood-onset SLE patients may also experience significant comorbidities (7-9). Previous studies have consistently shown higher comorbid conditions in late-onset SLE (10).

As a result, managing comorbid diseases has become an essential component of care in late-onset SLE, alongside disease-specific treatment. The objective of the present study was to examine the frequency and distribution of comorbidities by age at diagnosis in SLE patients followed at a tertiary rheumatology center over a one-year period.

CITATION

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MATERIAL AND METHOD

Selection of Patients

This was a retrospective, single-center study. We included SLE patients who presented to the Rheumatology Clinic at Gülhane Training and Research Hospital between February 2024 and February 2025. Patients were selected using International Classification of Diseases (ICD)-10 diagnosis codes from the hospital's electronic medical records. Individuals under the age of 18, those with repeated admissions, missing clinical data, or an unconfirmed diagnosis were excluded from the study. Only patients who met the revised 1990 American College of Rheumatology (ACR) SLE classification criteria were included. The study received ethical approval from the Institutional Review Board of Gülhane Training and Research Hospital, University of Health Sciences (Date: 06 May 2025; Decision number: 2025/272).

Clinical Information and Comorbidity Profile

Demographic and clinical data were retrieved from electronic medical system. Laboratory and autoantibody profiles were documented. Comorbid conditions were determined based on prior diagnoses, prescribed medications, and treatment history documented in the medical records. The following comorbidities were evaluated: arterial hypertension (HT), diabetes mellitus (DM), chronic kidney disease (CKD), autoimmune thyroid diseases, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD)/asthma, dyslipidemia, malignancy, osteopenia/osteoporosis, and avascular necrosis. The diagnoses of comorbid conditions were accurately documented, as were details of the patient's medical history, ICD-10 diagnosis codes, and prescribed medications.

Patients were categorized into three groups based on their age at diagnosis:

- Childhood-onset SLE (<18 years),
- Adult-onset SLE (18–49 years),
- Late-onset SLE (≥50 years) (11).

Statistical Analysis

The SPSS version 26.0 was used to perform for statistical analyses. Normality of variable distributions was assessed using both visual methods (histograms, normality plots) and analytical methods (Kolmogorov–Smirnov test). The chi-square test was used to compare and p-value <0.05 was considered statistically significant. One-way ANOVA and subsequent post hoc tests were used to compare groups affected by SLE and those with comorbid diseases.

RESULTS

284 patients with SLE were included in the study. The demographic and clinical characteristics of the patients were presented in Table 1. The mean age at diagnosis was 37.2 (±11.2) years, and 83.8% were female. The most common clinical manifestations were skin involvement (76.0%) and musculoskeletal involvement (69.7%). In total, 90.8% of patients had used hydroxychloroquine, and 58.8% had been treated with at least one immunosuppressive agent. Table 2 summarizes the comorbidities among all SLE patients.

Table 1. The demographic and clinical characteristics of patients with SLE

Demographic and clinical findings	All SLE patients n=284
Age at diagnosis, (SD)	37.2 (11.2)
Gender, female, n (%)	238 (83.8)
Disease duration, (SD)	9.3 (3.2)
Skin involvement, n (%) (acute cutaneous lupus, subacute cutaneous lupus, discoid lupus erythematosus, and lupus panniculitis)	216 (76.0)
Musculoskeletal involvement, n (%)	198 (69.7)
Alopecia, n (%)	99 (34.8)
Oral ulcers, n (%)	58 (20.4)
Renal involvement, n (%)	62 (21.8)
Hematological involvement, n (%)	44 (15.4)
Cardiac involvement, n (%)	4 (1.4)
Gastrointestinal involvement, n (%)	4 (1.4)
Neuropsychiatric involvement, n (%)	15 (5.2)
Serositis, n (%)	66 (23.2)
ANA test positivity, n (%)	264 (92.9)
Anti ds-DNA positivity, n (%)	234 (80.9)
ENA profile, ever, n (%)	
Anti-Sm, n (%)	82 (28.8)
Anti-RNP, n (%)	83 (29.2)
Anti-SSA, n (%)	108 (38)
Anti-SSB, n (%)	88 (30.9)
Anti-histon, n (%)	102 (35.9)
Anti-nucleosome, n (%)	97 (34.5)
Lymphopenia, n (%)	110 (38.7)
Low complement levels (C3,C4), n (%)	186 (65.4)
AFAS antibody positivity, n (%)	114 (40.1)
Glucocorticoid use, (ever), n (%)	224 (78.8)
Hydroxychloroquine use, (ever)	258 (90.8)
Immunosuppressive (IS) drug use (ever)	
1 IS	167 (58.8)
2 IS	54 (19)
IS 3 and above	19 (6.6)

ANA: antinuclear antibody, ds-DNA: double-stranded DNA, IS: immunosuppressive, SLE: systemic lupus erythematosus, SD: standard deviation

Table 2. Distribution of comorbid diseases in SLE patients

Comorbid diseases	All SLE patients n=284 (%)
Arterial hypertension	68 (23.9)
Diabetes mellitus	16 (5.6)
Dyslipidaemia	30 (10.5)
Coronary artery disease	13 (4.5)
Cardiac arrhythmias	16 (5.6)
Congestive heart failure	6 (2.1)
Chronic kidney disease	23 (8.0)
Cerebrovascular event	12 (4.2)
Osteoporosis	27 (9.5)
Avascular necrosis	11 (3.8)
Chronic obstructive pulmonary diseases	15 (5.2)
Autoimmune thyroid diseases	25 (8.8)
Malignancy	2 (0.7)

SLE: systemic lupus erythematosus

Table 2 shows the distribution of comorbid diseases in all SLE patients. The most common comorbid disease in patients with SLE was arterial hypertension (23.9%). Other frequently observed comorbidities were dyslipidaemia (10.5%) and osteoporosis (9.5%) respectively.

When stratified by age at diagnosis, 27 patients (7.1%) had childhood-onset SLE, 176 (61.9%) had adult-onset SLE, and 81 (28.5%) had late-onset SLE. Arterial HT was significantly more frequent in the late-onset SLE group compared to other groups (46.9% vs. 15.9% and 7.4%, respectively; p_1=0.004, p_2=0.0021). Similarly, osteoporosis was more prevalent (22.2% vs. 4.5% and 3.7%; p_1=0.014, p_2=0.032). No statistically significant differences was observed among the groups in other comorbidities. Table 3 details the distribution of comorbidities according to SLE groups.

Table 3. Differences of comorbid diseases in childhood SLE, adult onset SLE, late onset SLE

Comorbid diseases	Childhood-onset SLE <18years n=27 (%)	Adult-onset SLE (18-49 years) n=176 (%)	Late-onset SLE ≥50 years n=81 (%)	p*
Arterial Hypertension	2 (7.4)	28 (15.9)	38 (46.9)	<0.001
Diabetes Mellitus	0	7 (3.9)	9 (11.1)	0.27
Dyslipidaemia	0	11 (6.2)	19 (23.4)	0.063
Chronic kidney disease	2 (7.4)	10 (5.6)	11 (13)	0.73
Coronary Artery Disease	0	6 (3.4)	7 (8.6)	0.87
Congestive heart failure	0	1 (0.5)	5 (6.2)	0.61
Cerebrovascular event	1 (3.7)	3 (1.7)	8(18.5)	0.06
Osteoporosis	1 (3.7)	8 (4.5)	18 (22.2)	0.022
Avascular necrosis	1 (3.7)	6 (3.4)	4 (4.9)	0.42
Chronic obstructive pulmonary diseases	1 (3.7)	10 (5.7)	4 (4.9)	0.60
Autoimmune thyroid diseases	6 (22.2)	11 (6.2)	8 (9.8)	0.06
Malignancy	0	1 (0.5)	1 (1.2)	0.43

SLE: systemic lupus erythematosus; *p1 Comparision between late onset SLE and adult onset SLE, p2 Comparision between late onset SLE and childhood SLE

DISCUSSION

In our study, arterial hypertension emerged as the most common comorbidity among SLE patients (23.9%), with a significantly higher prevalence in the late-onset SLE group. Osteoporosis was also notably more frequent. Contrariwise, autoimmune thyroid diseases were more prevalent in childhood-onset SLE.

Arterial HT is more prevalent among patients with SLE than in the general population, according to previous studies (12,13). Bruce IN. et al. found HT rate of 33% among 250 SLE patients, than controls (13%) (p=0.001) (14). Similarly, a large study involving 1042 SLE patients reported a 20.8% HT prevalence (8). The prevalence of HT in late-onset patients was 46.9%, compared to 15.9% in adult-onset patients (p<0.001) in our SLE patients. These findings were similar with Riveros Frutos A. et al., who found HT in 51.6% of late-onset versus 25.1% of adult-onset patients (15). Kang JH. et al. also reported higher rates in Korean late-onset SLE patients (24 vs 4%) (16). Studies have emphasized that the frequency of HT is not increased in age- and gender-matched SLE patients. It has been suggested that age may be a contributing factor to the development of high arterial HT in late-onset SLE patients (17).

In our study, osteoporosis was observed in 8.8% of all patients and in 22.2 % of those with late-onset SLE. Yee et al. reported a 10.3% osteoporosis rate among 242 SLE patients (18). In a study using a 45-year cutoff for late-onset, osteoporosis was observed in 11.4% of patients, with significantly higher rates compared to adult-onset patients (9). Another study comparing 73 late-onset and 144 adult-onset patients found higher osteoporosis prevalence in the late-onset SLE (9.5% vs. 0.6%, p=0.017) (19). Our findings support the conclusion that osteoporosis is more frequent.

We found thyroid diseases in 9.1% of all SLE patients, with the highest frequency in childhood-onset SLE (22.2%), compared to 6.2% in adult-onset and 9.8% in late-onset SLE. The small size of the childhood-onset group (n=27) might be a contributing factor in our study. A prior study of 524 SLE patients reported thyroid disease in 6.1% (20). While some studies found no significant differences across age groups (21), Tomic-Lucic A. et al. found slightly increased rate of hypothyroidism in early-onset SLE (10% vs. 3.3%) (22).

In our study, DM was observed to be slightly more prevalent in late-onset patients (11.1%) compared to other groups (3.9% and 0%, p=0.27). Other studies have reported varying results. It is reported by Ward MM. et al. that 14.7% of DM occurs in cases of late-onset SLE and 4.3% in cases of childhood-onset SLE (23). In contrast, the findings of Bertoli AM. et al. indicated a higher DM prevalence in adult-onset compared to late-onset SLE (10.9% vs. 0.69%, p=0.01) (20). Das Chagas Medeiros MM. et al. found a DM prevalence of 13.3% in late-onset and 8.2% in adult-onset patients, though the difference was not statistically significant (21).

Several limitations are presented by this study. Due to its retrospective design, data on potential confounders such as disease activity scores could not be consistently captured. In late-onset patients, cumulative glucocorticoid

exposure may have contributed to osteoporosis and steroid-induced diabetes, but this could not be quantified. Our study highlights into the age-related distribution of comorbidities among SLE patients in a real-world tertiary care setting.

CONCLUSION

Arterial HT and osteoporosis may be present in late-onset SLE compared to those with earlier-onset disease. The presence of comorbid conditions in this subgroup may significantly impact organ damage. Therefore, in addition to disease-specific management, addressing comorbidities should be managed in late-onset SLE to improve clinical outcomes.

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