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ORIGINAL RESEARCH

Gender-Related Differences in the Clinical, Immunological, and Treatment Characteristics of Patients with Systemic Lupus Erythematosus

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ABSTRACT

This retrospective study aimed to evaluate sex-related differences in the clinical, laboratory, immunological, and treatment characteristics of patients with systemic lupus erythematosus (SLE) at a single tertiary center. The study included 68 SLE patients (34 females and 34 males) of similar ages at diagnosis, whose data were retrieved from electronic medical records between 2010 and 2025. Clinical manifestations, comorbidities, serological profiles, organ involvement, disease activity (SLEDAI), and treatment regimens were analyzed, and statistical analyses were performed using R software. The most frequent initial complaints in males were constitutional, cutaneous, and musculoskeletal symptoms, whereas musculoskeletal and cutaneous symptoms predominated in females. Leg swelling, as an initial manifestation, and renal involvement during disease progression were more frequent in males ($p=0.029$). Serologically, anti-double-stranded DNA, anti-cardiolipin IgG, and lupus anticoagulant positivity were higher in males, while complement C3 and C4 levels were lower in females ($p<0.05$ for all). Additionally, sicca symptoms, Raynaud's phenomenon, livedo reticularis, and musculoskeletal involvement were more common in females, and intravenous methylprednisolone and cyclophosphamide use was more frequent in males. Although SLEDAI scores were higher in males, the difference was not statistically significant, and overall disease patterns were largely similar between sexes; however, male patients exhibited a higher frequency of renal involvement, accompanied by more frequent use of aggressive immunosuppressive treatment. These findings emphasize the importance of considering sex-specific differences in the clinical assessment, monitoring, and management of SLE patients.

Keywords: Males. Sex. Systemic Lupus Erythematosus.

Sistemik Lupus Eritematozus Hastalarında Klinik, İmmünolojik ve Tedavi Özelliklerinde Cinsiyete Bağlı Farklılıklar

ÖZET

Bu çalışma, tek bir üçüncü basamak merkezde takip edilen sistemik lupus eritematozus (SLE) hastalarının klinik, laboratuvar, immünolojik ve tedavi özelliklerindeki cinsiyete bağlı farklılıkları değerlendirmek amacıyla yapılmıştır. Bu retrospektif çalışmaya, tanı anındaki yaşları benzer 68 SLE hastası (34 kadın, 34 erkek) dahil edilmiştir. Veriler, 2010 ile 2025 yılları arasında elektronik hasta kayıtlarından elde edilmiştir. Klinik belirtiler, komorbiditeler, serolojik profiller, organ tutulumları, hastalık aktivitesi (SLEDAI) ve tedavi rejimleri analiz edildi. İstatistiksel analizler R yazılımı kullanılarak gerçekleştirildi. En sık görülen ilk şikayetler erkeklerde konstitüsyonel semptomlar, cilt belirtileri ve kas-iskelet sistemi semptomları iken, kadınlarda kas-iskelet sistemi semptomları ve cilt belirtileri idi. Erkek hastalarda ilk semptom olarak bacak şişliği oranları anlamlı olarak daha yüksekti ve hastalık seyri boyunca böbrek tutulum sıklığı daha fazlaydı ($p=0,029$). Serolojik olarak, çift sarmallı DNA'ya karşı antikor, anti-kardiyolipin IgG ve lupus antikoagülan pozitifliği erkeklerde anlamlı olarak daha yüksekken, kompleman C3 ve C4 düzeyleri kadınlarda daha düşüktü (hepsi için $p<0,05$). Sikka semptomları, Raynaud fenomeni, livedo retikularis ve kas-iskelet sistemi tutulumları kadınlarda daha sık görüldü. İntravenöz metilprednizolon ve siklofosfamid kullanımı erkeklerde anlamlı olarak daha yüksekti. Klinik SLEDAI skorları erkeklerde daha yüksek olmasına rağmen, bu fark istatistiksel olarak anlamlı değildi. Genel hastalık paternleri cinsiyetler arasında büyük ölçüde benzer olsa da, erkek SLE hastalarında böbrek tutulum sıklığı daha yüksekti, bu da agresif immünosüpresif tedaviye olan ihtiyacı artırdı. Bu bulgular, SLE yönetimi ve takip stratejilerinde cinsiyete dayalı farklılıkların önemini vurgulamaktadır.

Anahtar Kelimeler: Cinsiyet. Erkek. Sistemik Lupus Eritematozus.

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Systemic lupus erythematosus (SLE) is a chronic, autoimmune, and inflammatory rheumatic disease characterized by multisystem involvement and female predominance[1,2]. The female-to-male ratio varies widely across populations, ranging from 1.2:1 to 15:1 worldwide[3]. Serologically, SLE is characterized by the presence of autoantibodies directed against self-antigens, particularly antinuclear antibodies (ANAs), and several genetic and environmental factors contribute to its onset and progression, leading to a highly heterogeneous clinical course. Multiorgan involvement is common in SLE and is a major contributor to disease-related morbidity and mortality[4-7], and numerous studies have evaluated clinical manifestations and autoantibody profiles in male and female SLE patients[2,5,8]. Although findings vary across studies, male patients have been reported to exhibit higher rates of renal involvement, serositis, and cardiovascular complications. In addition, lupus anticoagulant positivity (LA), anti-double-stranded DNA (anti-dsDNA) positivity, and lower complement levels have been reported more frequently in males. Most studies also suggest that male patients tend to have a more severe disease course, greater organ damage, and a poorer response to treatment compared to females[6,9,10]. However, because the clinical expression of SLE may differ across patient populations and healthcare settings, further data from different cohorts remain valuable. Therefore, the present study aims to evaluate the demographic, clinical, immunological, and treatment characteristics of SLE patients followed at our center, with a particular focus on the influence of sex on these parameters.

Materials and Methods

This retrospective, single-center study was approved by the Ethics Committee of Bursa Uludağ University's Faculty of Medicine (approval date: November 4, 2020; approval number: 2020-19/31) and was conducted in accordance with the principles of the Declaration of Helsinki. Data from patients diagnosed with SLE and followed at the rheumatology outpatient clinic of Bursa Uludağ University's Faculty of Medicine between January 2010 and March 2025 were retrospectively retrieved through the hospital electronic medical record system and reviewed. A total of 435 female and 50 male patients were screened. Among the male patients, 34 fulfilled the inclusion criteria and had complete medical records. Female patients were selected from the larger cohort using frequency matching according to age at diagnosis to obtain a comparable age-at-diagnosis distribution with the male group. The inclusion criteria were age ≥18 years and a confirmed diagnosis of SLE, while patients with incomplete or missing medical records were excluded from the study. SLE diagnosis was established according to the 1997 American College of Rheumatology (ACR), 2012 Systemic Lupus International Collaborating Clinics (SLICC), and 2019 European League Against Rheumatism (EULAR)/ACR classification criteria at the time of diagnosis, and disease activity at the last visit was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI).

Screening data

The following variables were recorded: 1) sex (female or male) and age (years); 2) follow-up characteristics (regular follow-up status, age at diagnosis [years], whether age at diagnosis was above or below 18 years, and time since diagnosis [months]); 3) presence of comorbidities (diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, heart failure, hypothyroidism, and hyperthyroidism), antiphospholipid syndrome (APS), sicca syndrome, a history of miscarriage, stillbirth, and additional conditions such as avascular necrosis, malignancy, kidney transplantation, and liver transplantation; 4) initial complaints (the first symptom occurring at disease onset) (neck swelling, constitutional symptoms, dry mouth, dry eyes, skin manifestations [alopecia, rash, and malar rash], joint manifestations, dyspnea, palpitations, chest pain, leg swelling, Raynaud's syndrome, complaints related to thrombosis and bleeding, and neurological symptoms [cerebrovascular event and foot drop]); 5) laboratory tests (EBV IgG or IgM, ANA, anti-histone antibody, anti-nucleosome antibody, anti-centromere antibody, Ribosomal P Protein Antibody [anti-Ribosomal-p], Anti-Sjögren Syndrome Antibody A [anti-SS-A], Anti-Sjögren Syndrome Antibody B [anti-SS-B], systemic lupus erythematosus antibody [anti-Sm], nucleolar ribonucleoprotein antibody [anti-Sm/RNP], anti-dsDNA, anti-cardiolipin IgM, anti-cardiolipin IgG, anti-beta2glycoprotein IgM, anti-beta2glycoprotein IgG antibodies, LA, complement

C3, and complement C4); 6) history of biopsy from any tissue or organ (renal biopsy, skin biopsy, bone marrow biopsy, salivary gland biopsy, lung parenchymal biopsy, or liver parenchymal biopsy); 7) clinical manifestations during the entire disease course (sicca symptoms, constitutional symptoms [fever, weight loss, and fatigue], peritonitis, musculoskeletal manifestations [arthralgia, arthritis, and myalgia], cardiac involvement [pericarditis, pericardial effusion, and acute coronary syndrome], hematological manifestations [lymphopenia, autoimmune hemolytic anemia, anemia, and thrombocytopenia], mucocutaneous manifestations [oral aphthae, genital ulcer, alopecia, purpura, livedo reticularis, vasculitic rash, SLE-specific rash, malar rash, and photosensitivity], neurological involvement, renal involvement [renal involvement was defined as the presence of lupus-related proteinuria and/or acute renal injury, with or without biopsy-confirmed lupus nephritis], pulmonary involvement [pleuritis, interstitial pneumonia, pulmonary vasculitis, interstitial fibrosis, pulmonary hypertension, pleural effusion, and infection], and vascular involvement [Raynaud's syndrome, thrombosis, embolism, and deep vein thrombosis]); 8) SLEDAI score at the last visit; and 9) total treatments (hydroxychloroquine [HCQ], oral prednisolone, oral methylprednisolone, intravenous methylprednisolone [MP IV], intravenous cyclophosphamide [CYC IV], azathioprine, methotrexate, mycophenolate mofetil, rituximab, warfarin, low molecular weight heparin, and tacrolimus).

Statistical analysis

Data were analyzed using R software. The normality of data distribution was assessed using the Shapiro–Wilk test, and Yates' correction and Fisher's exact test were used to examine the association between categorical variables. The Mann–Whitney U test was used for the analysis of non-normally distributed data between two groups, while the independent samples t-test was used to compare normally distributed data between two groups. The results were presented as means ± standard deviations or medians (minimum–maximum) for quantitative variables, and categorical variables were expressed as frequencies and percentages. A p-value of <0.05 was considered statistically significant.

Results

A total of 68 SLE patients were included in the study, of whom 34 (50%) were male. The mean age at diagnosis was 31.41 ± 11.53 (mean ± standard deviation) years in males and 29.26 ± 10.26 years in females, and the mean time since diagnosis was 116.24 ± 77.47 months in males and 181.06 ± 95.97 months in females. In both male and female groups, 30 patients (88.2%) were diagnosed at ≥18 years of age, while four patients (11.8%) were diagnosed before the age of 18. The proportion of exitus was 26.5% in males and 14.7% in females, and the rate of regular follow-up was 38.2% in males and 52.9% in females. There were no statistically significant differences between males and females in terms of age at diagnosis, categorical age at diagnosis, presence of exitus and regular follow-up status ($p=0.422$, 1.000, 0.810, and 0.330, respectively). However, time since diagnosis was significantly higher in females ($p=0.003$).

The characteristics of male and female patients in terms of comorbidities during the disease course are presented in Table I. There were no statistically significant differences between male and female groups in terms of diabetes mellitus, hyperlipidemia, coronary artery disease, heart failure, hypothyroidism, hyperthyroidism, APS, and sicca syndrome ($p>0.05$). However, the overall presence of comorbidities and hypertension were significantly higher in females ($p=0.014$ and $p=0.020$, respectively). A history of miscarriage was present in four (11.8%) female patients, while three (8.8%) had a history of stillbirth. During follow-up, three (8.8%) male patients had avascular necrosis, two (5.9%) male patients had undergone kidney transplantation, one (2.9%) male patient had undergone liver transplantation, one (2.9%) female patient had undergone bone marrow transplantation, and four (11.8%) female patients had a history of malignancy.

The characteristics of male and female patients in terms of initial complaints are presented in Table I. Initial complaints, constitutional symptoms (58.8%), cutaneous manifestations (55.9%), and musculoskeletal complaints (50%) were most frequently observed in male patients, whereas musculoskeletal complaints (70.6%) and cutaneous manifestations (61.8%) were most frequent in female patients. However, there were no statistically significant differences between male and female groups in terms of initial complaints, including neck swelling, constitutional symptoms, dry mouth, dry eyes, skin manifestations, musculoskeletal findings, dyspnea, palpitations and chest pain, Raynaud's symptoms, thrombotic-related complaints, bleeding-related complaints, and neurological symptoms ($p>0.05$). However, the presence of leg swelling as an initial complaint was significantly higher in males ($p=0.010$).

Laboratory findings at the time of diagnosis are presented in Table I. Anti-dsDNA (79.4%) was the most frequently positive antibody in male patients, while anti-SS-A (39.4%) was the most frequent in female patients. There were no statistically significant

Table I. Comparison of demographic, clinical, laboratory, and treatment characteristics between male and female patients

		Male (n=34)			Female (n=34)			Whole group (n=68)			p-value*
		Mean ± SD / n (%) / Median (min–max)									
CHARACTERISTICS OF PATIENTS											
Age at diagnosis		31.41±11.63			29.26±10.26			30.34 ± 10.94			0.422 t
Time since diagnosis (months)		116.24±77.47			181.06±95.94			148.65 ± 92.51			0.003 t
SLEDAI Scores at the last visit				6 (0–20)			3 (0–22)			4.5 (0–22)	0.374 m
Survival	Dead	9	26.5%		5	14.7%		14	20.6%		0.368 x
	Alive	25	73.5%		29	85.3%		54	79.4%		
Regular follow-up	No	21	61.8%		16	47.1%		37	54.4%		0.330 x
	Yes	13	38.2%		18	52.9%		31	45.6%		
Age at diagnosis category	18≤	30	88.2%		30	88.2%		60	88.2%		1.000 y
	18>	4	11.8%		4	11.8%		8	11.8%		
COMORBIDITIES											
General	No	25	73.5%		14	41.2%		39	57.4%		0.014 x
	Yes	9	26.5%		20	58.8%		29	42.7%		
Diabetes mellitus	No	34	100%		29	85.3%		63	92.7%		0.053 y
	Yes	0	0%		5	14.7%		5	7.4%		
Hypertension	No	28	82.4%		18	52.9%		46	67.7%		0.020 x
	Yes	6	17.7%		16	47.1%		22	32.4%		
Hyperlipidemia	No	33	97.1%		32	94.1%		65	95.6%		1.000 y
	Yes	1	2.9%		2	5.9%		3	4.4%		
Coronary artery disease	No	32	94.1%		29	85.3%		61	89.7%		0.428 y
	Yes	2	5.9%		5	14.7%		7	10.3%		
Heart failure	No	31	91.2%		33	97.1%		64	94.1%		0.614 y
	Yes	3	8.8%		1	2.9%		4	5.9%		
Hypothyroidism	No	32	94.1%		31	91.2%		63	92.7%		1.000 y
	Yes	2	5.9%		3	8.8%		5	7.4%		
Hyperthyroidism	No	34	100%		33	97.1%		67	98.5%		1.000 y
	Yes	0	0%		1	2.9%		1	1.5%		
APS	No	28	82.4%		29	85.3%		57	83.8%		1.000 y
	Yes	6	17.7%		5	14.7%		11	16.2%		
Secondary Sjögren syndrome	No	30	88.2%		24	70.6%		54	79.4%		0.134 x
	Yes	4	11.8%		10	29.4%		14	20.6%		
Miscarriage	No	33	100%		30	88.2%		63	94%		0.114 y
	Yes	0	0%		4	11.8%		4	6%		
Stillbirth	No	34	100%		31	91.2%		65	95.6%		0.239 y
	Yes	0	0%		3	8.8%		3	4.4%		
INITIAL COMPLAINTS											
Neck swelling	No	34	100%		33	97.1%		67	98.5%		1.000 y
	Yes	0	0%		1	2.9%		1	1.5%		
Constitutional symptoms	No	14	41.2%		23	67.7%		37	54.4%		0.051 y
	Yes	20	58.8%		11	32.4%		31	45.6%		
Sicca symptoms	No	26	76.5%		28	82.4%		54	79.4%		0.764 x
	Yes	8	23.5%		6	17.7%		14	20.6%		
Alopecia, rash, malar rash	No	15	44.1%		13	38.2%		28	41.2%		0.805 x
	Yes	19	55.9%		21	61.8%		40	58.8%		
Musculoskeletal manifestations	No	17	50%		10	29.4%		27	39.7%		0.137 x
	Yes	17	50%		24	70.6%		41	60.3%		
Dyspnea	No	26	76.5%		28	82.4%		54	79.4%		0.764 x
	Yes	8	23.5%		6	17.7%		14	20.6%		
Palpitations, chest pain	No	32	94.1%		31	91.2%		63	92.7%		1.000 y
	Yes	2	5.9%		3	8.8%		5	7.4%		
Leg swelling	No	21	61.8%		31	91.2%		52	76.5%		0.010 x
	Yes	13	38.2%		3	8.8%		16	23.5%		
Raynaud	No	30	88.2%		28	82.4%		58	85.3%		0.732 x
	Yes	4	11.8%		6	17.7%		10	14.7%		
Thrombotic-related	No	23	67.7%		29	85.3%		52	76.5%		0.153 x
	Yes	11	32.4%		5	14.7%		16	23.5%		
Bleeding-related	No	30	88.2%		33	97.1%		63	92.7%		0.356 y
	Yes	4	11.8%		1	2.9%		5	7.4%		
Neurological symptoms	No	32	94.1%		33	97.1%		65	95.6%		1.000 y
	Yes	2	5.9%		1	2.9%		3	4.4%		
LABORATORY											
ANA	No	2	5.9%		2	6.1%		4	6%		1.000 y
	Yes	32	94.1%		31	93.9%		63	94%		
Anti-histone antibody	No	22	66.7%		28	84.9%		50	75.8%		0.151 x
	Yes	11	33.1%		5	15.2%		16	24.2%		
Anti-nucleosome antibody	No	12	48%		23	74.2%		35	62.5%		0.083 x
	Yes	13	52%		8	25.8%		21	37.5%		

Table I. Continued

Anti-centromere antibody	No	28	87.5%		33	100%		61	93.9%		0.353 [y]
	Yes	4	12.5%		0	0%		4	6.2%		
Anti-Ribosomal-p	No	24	75%		26	78.8%		50	76.9%		0.946 [x]
	Yes	8	25%		7	21.2%		15	23.1%		
Anti-SS-A	No	21	65.6%		20	60.6%		41	63.1%		0.871 [x]
	Yes	11	34.4%		13	39.4%		24	36.9%		
Anti-SS-B	No	28	87.5%		28	84.9%		56	86.2%		1.000 [y]
	Yes	4	12.5%		5	15.2%		9	13.9%		
Anti-Sm	No	25	78.1%		28	84.9%		53	81.5%		0.705 [x]
	Yes	7	21.9%		5	15.2%		12	18.5%		
Anti-Sm/RNP	No	25	75.8%		26	78.8%		51	77.3%		1.000 [x]
	Yes	8	24.2%		7	21.2%		15	22.7%		
Anti-dsDNA	No	7	20.6%		21	63.6%		28	41.8%		<0.001 [x]
	Yes	27	79.4%		12	36.4%		39	58.2%		
Complement C3	No	19	55.9%		5	16.7%		24	37.5%		0.003 [x]
	Yes	15	44.1%		25	83.3%		40	62.5%		
Complement C4	No	15	44.1%		3	10%		18	28.1%		0.006 [x]
	Yes	19	55.9%		27	90%		46	71.9%		
aCL IgG	No	14	56%		27	93.1%		41	75.9%		0.004 [x]
	Yes	11	44%		2	6.9%		13	24.1%		
LA	No	7	43.8%		13	92.9%		20	66.7%		0.007 [y]
	Yes	9	56.3%		1	7.1%		10	33.3%		
Anti-β2GPI IgG	No	6	100%		3	60%		9	81.8%		0.182 [y]
	Yes	0	0%		2	40%		2	18.2%		
CLINICAL MANIFESTATIONS DURING FOLLOW-UP											
Sicca	No	25	73.5%		13	38.2%		38	55.9%		0.007 [x]
	Yes	9	26.5%		21	61.8%		30	44.1%		
Total constitutional symptoms	No	13	38.2%		15	44.1%		28	41.2%		0.805 [x]
	Yes	21	61.8%		19	55.9%		40	58.8%		
Fever	No	29	85.3%		32	94.1%		61	89.7%		0.428 [y]
	Yes	5	14.7%		2	5.9%		7	10.3%		
Weight loss	No	26	76.5%		28	82.4%		54	79.4%		0.764 [x]
	Yes	8	23.5%		6	17.7%		14	20.6%		
Fatigue	No	14	41.2%		17	50%		31	45.6%		0.626 [x]
	Yes	20	58.8%		17	50%		37	54.4%		
Peritonitis	No	33	91.1%		31	91.2%		64	94.1%		0.614 [y]
	Yes	1	2.9%		3	8.8%		4	5.9%		
Total musculoskeletal manifestations	No	12	35.3%		3	8.8%		15	22.1%		0.019 [x]
	Yes	22	64.7%		31	91.2%		53	77.9%		
Arthralgia	No	11	32.4%		3	8.8%		14	20.6%		0.036 [x]
	Yes	23	67.7%		31	91.2%		54	79.4%		
Arthritis	No	18	52.9%		17	50%		35	51.5%		1.000 [x]
	Yes	16	47.1%		17	50%		33	48.5%		
Myalgia	No	24	70.6%		18	52.9%		42	61.8%		0.212 [x]
	Yes	10	29.4%		16	47.1%		26	38.2%		
Total cardiac manifestations	No	31	91.2%		29	85.3%		60	88.2%		0.709 [y]
	Yes	3	8.8%		5	14.7%		8	11.8%		
Pericardial effusion	No	32	94.1%		29	85.3%		61	89.7%		0.428 [y]
	Yes	2	5.9%		5	14.7%		7	10.3%		
Acute coronary syndrome	No	32	94.1%		34	100%		66	97.1%		0.493 [y]
	Yes	2	5.9%		0	0%		2	2.9%		
Total hematological manifestations	No	17	50%		20	58.8%		37	54.4%		0.626 [x]
	Yes	17	50%		14	41.2%		31	45.6%		
Lymphopenia	No	18	52.9%		24	70.6%		42	61.8%		0.212 [x]
	Yes	16	47.1%		10	29.4%		26	38.2%		
Autoimmune hemolytic anemia	No	31	91.2%		32	94.1%		63	92.7%		1.000 [y]
	Yes	3	8.8%		2	5.9%		5	7.4%		
Anemia	No	18	52.9%		22	64.7%		40	58.8%		0.460 [x]
	Yes	16	47.1%		12	35.3%		28	41.2%		
Thrombocytopenia	No	25	73.5%		28	82.4%		53	77.9%		0.559 [x]
	Yes	9	26.5%		6	17.7%		15	22.1%		
Total mucocutaneous manifestations	No	12	35.3%		6	17.7%		18	26.5%		0.169 [x]
	Yes	22	64.7%		28	82.4%		50	73.5%		
Oral aphthae	No	31	91.2%		28	82.4%		59	86.8%		0.476 [y]
	Yes	3	8.8%		6	17.7%		9	13.2%		
Genital ulcer	No	34	100%		33	97.1%		67	98.5%		1.000 [y]
	Yes	0	0%		1	2.9%		1	1.5%		
Alopecia	No	25	73.5%		17	50%		42	61.8%		0.081 [x]
	Yes	9	26.5%		17	50%		26	38.2%		
Purpura	No	29	85.3%		33	97.1%		62	91.2%		0.197 [y]
	Yes	5	14.7%		1	2.9%		6	8.8%		

Table I. Continued

Livedo reticularis	No	34	100%		28	82.4%		62	91.2%		0.025 [y]
	Yes	0	0%		6	17.7%		6	8.8%		
Vasculitic rash	No	31	91.2%		32	94.1%		63	92.7%		1.000 [y]
	Yes	3	8.8%		2	5.9%		5	7.4%		
SLE-specific rash	No	20	58.8%		22	64.7%		42	61.8%		0.803 [x]
	Yes	14	41.2%		12	35.3%		26	38.2%		
Malar rash	No	29	85.3%		21	61.8%		50	73.5%		0.054 [x]
	Yes	5	14.7%		13	38.2%		18	26.5%		
Photosensitivity	No	26	76.5%		23	67.7%		49	72.1%		0.589 [x]
	Yes	8	23.5%		11	32.4%		19	27.9%		
Total neurological involvement	No	32	94.4%		33	97.1%		65	95.6%		1.000 [y]
	Yes	2	5.9%		1	2.9%		3	4.4%		
Total renal involvement	No	12	35.3%		22	64.7%		34	50%		0.029 [x]
	Yes	22	64.7%		12	35.3%		34	50%		
Acute renal injury	No	30	88.2%		31	91.2%		61	89.7%		1.000 [y]
	Yes	4	11.8%		3	8.8%		7	10.3%		
Proteinuria	No	13	38.2%		22	64.7%		35	51.5%		0.052 [x]
	Yes	21	61.8%		12	35.3%		33	48.5%		
Total pulmonary involvement	No	27	79.4%		23	67.7%		50	73.5%		0.410 [x]
	Yes	7	20.6%		11	32.4%		18	26.5%		
Pleuritis	No	28	82.4%		30	88.2%		58	85.3%		0.732 [x]
	Yes	6	17.7%		4	11.8%		10	14.7%		
Interstitial pneumonia	No	32	94.1%		33	97.1%		65	95.6%		1.000 [y]
	Yes	2	5.9%		1	2.9%		3	4.4%		
Pulmonary vasculitis	No	32	94.1%		33	97.1%		65	95.6%		1.000 [y]
	Yes	2	5.9%		1	2.9%		3	4.4%		
Interstitial fibrosis	No	34	100%		33	97.1%		67	98.5%		1.000 [y]
	Yes	0	0%		1	2.9%		1	1.5%		
Pulmonary hypertension	No	32	94.1%		32	94.1%		64	94.1%		1.000 [y]
	Yes	2	5.9%		2	5.9%		4	5.9%		
Pleural effusion	No	29	85.3%		23	67.7%		52	76.5%		0.153 [x]
	Yes	5	14.7%		11	32.4%		16	23.5%		
Infection	No	26	76.5%		29	85.3%		55	80.9%		0.537 [x]
	Yes	8	23.5%		5	14.7%		13	19.1%		
Total vascular involvement	No	20	58.8%		16	47.1%		36	52.9%		0.466 [x]
	Yes	14	41.2%		18	52.9%		32	47.1%		
Raynaud	No	30	88.2%		21	61.8%		51	75%		0.025 [x]
	Yes	4	11.8%		13	38.2%		17	25%		
Thrombosis	No	27	79.4%		28	82.4%		55	80.9%		1.000 [x]
	Yes	7	20.6%		6	17.7%		13	19.1%		
TREATMENT DURING FOLLOW-UP											
Oral Prednisolone	No	5	14.7%		3	8.8%		8	11.8%		0.709 [y]
	Yes	29	85.3%		31	91.2%		60	88.2%		
Oral Methylprednisolone	No	23	67.7%		25	73.5%		48	70.6%		0.790 [x]
	Yes	11	32.4%		9	26.5%		20	29.4%		
Intravenous Methylprednisolone	No	11	32.4%		29	85.3%		40	58.8%		0.001 [x]
	Yes	23	67.7%		5	14.7%		28	41.2%		
Intravenous Cyclophosphamide	No	13	38.2%		25	73.5%		38	55.9%		0.007 [x]
	Yes	21	61.8%		9	26.5%		30	44.1%		
Azathioprine	No	13	38.2%		16	47.1%		29	42.7%		0.624 [x]
	Yes	21	61.8%		18	52.9%		39	57.4%		
Methotrexate	No	29	85.3%		23	67.7%		52	76.5%		0.153 [x]
	Yes	5	14.7%		11	32.4%		16	23.5%		
Mycophenolate mofetil	No	17	50%		23	67.7%		40	58.8%		0.218 [x]
	Yes	17	50%		11	32.4%		28	41.2%		
Rituximab	No	27	79.4%		29	85.3%		56	82.4%		0.750 [x]
	Yes	7	20.6%		5	14.7%		12	17.7%		
Warfarin	No	28	82.4%		31	91.2%		59	86.8%		0.476 [y]
	Yes	6	17.7%		3	8.8%		9	13.2%		
Low molecular weight heparin	No	26	76.5%		27	79.4%		53	77.9%		1.000 [x]
	Yes	8	23.5%		7	20.6%		15	22.1%		
Tacrolimus	No	34	100%		33	97.1%		67	98.5%		1.000 [y]
	Yes	0	0%		1	2.9%		1	1.5%		
Intravenous Immunoglobulin	No	32	94.1%		34	100%		66	97.1%		0.493 [y]
	Yes	2	5.9%		0	0%		2	2.9%		

APS: Antiphospholipid antibody syndrome; ANA: antinuclear antibody; anti-β2GPI IgG: anti-beta2glycoprotein IgG antibody; Anti-dsDNA: double-stranded DNA antibody; anti-Ribosomal-p: Ribosomal P protein antibody; anti-Sm: Systemic Lupus Erythematosus antibody; anti-Sm/RNP: nucleolar ribonucleoprotein antibody; anti-SS-A: anti-Sjögren Syndrome antibody A; anti-SS-B: anti-Sjögren Syndrome antibody B; aCL IgG: anti-cardiolipin IgG; LA: lupus anticoagulant. * The p-value indicates the statistical significance between the male and female groups. [x] Yates correction/ [y] Fisher's Exact test/ [m] Mann Whitney U test/ [t] Independent samples t test.

differences between male and female groups in terms of ANA, anti-histone, anti-nucleosome, anti-centromere, anti-Ribosomal-p, anti-SS-A, anti-SS-B, anti-Sm, anti-Sm/RNP, anti-cardiolipin IgM, anti-beta2glycoprotein IgM, and anti-beta2glycoprotein IgG antibodies (p>0.05). Anti-dsDNA, anti-cardiolipin IgG, and lupus anticoagulant antibodies were significantly higher in males (p=<0.001, 0.004, and 0.007, respectively), whereas complement C3 and C4 levels were significantly lower in females (p=0.003 and 0.006, respectively). Six (28.6%) male patients and one (5%) female patient had a history of EBV infection.

Nineteen (55.9%) male and twelve (35.3%) female patients had a history of biopsy performed from any site during the course of their disease. Renal biopsy was performed in twelve (36.4%) male and eight (23.5%) female patients. Skin and bone marrow biopsies were performed in three (8.8%) male and three (8.8%) female patients. Salivary gland biopsy was performed in one (2.9%) male and three (8.8%) female patients. Additionally, lung biopsy was performed in one (2.9%) male patient and liver biopsy in one (2.9%) male patient.

Clinical findings, symptoms, and organ involvement during the entire disease course are presented in Table I. The most common symptom in both male and female patients was arthralgia (67.7% and 91.2%, respectively). In males, musculoskeletal system involvement, mucocutaneous manifestations, and renal involvement were observed in 64.7% of patients, while musculoskeletal system involvement, mucocutaneous manifestations, and sicca symptoms were observed in 91.2%, 82.4%, and 61.8% of female patients, respectively. Renal involvement was observed in 22 male (64.7%) and 12 female (35.3%) patients and was significantly higher in males (p=0.029). Conversely, sicca symptoms, musculoskeletal system involvement, arthralgia, livedo reticularis, and Raynaud's syndrome were significantly more frequent in females (p values=0.007, 0.019, 0.036, 0.025, and 0.025, respectively).

The median SLEDAI score at the last visit was 6 (0–20) in males and 3 (0–22) in females, and there was no statistically significant difference between the groups in terms of SLEDAI scores (p=0.374).

Treatments throughout the entire disease course are presented in Table I, with all male and female patients receiving HCQ, and MP IV and CYC IV use was significantly higher in males (p=<0.001 and 0.007, respectively).

Discussion and Conclusion

In this study, differences in demographic characteristics, antibody profiles, initial complaints, clinical course, and treatment approaches between male and female SLE patients were evaluated. Our findings indicate that leg swelling as an initial complaint was more frequent in male patients and that renal involvement was more prevalent in males in terms of overall disease manifestations. In addition, anti-dsDNA, anti-cardiolipin IgG, and lupus anticoagulant antibodies were more frequently elevated in males. In contrast, sicca symptoms, musculoskeletal manifestations, arthralgia, livedo reticularis, and Raynaud's phenomenon were more commonly observed in female patients. Serologically, decreased complement C3 and C4 levels were more frequently detected in females.

The age at diagnosis was similar between male and female groups, with the mean age being 31.41 ± 11.53 years in males and 29.26 ± 10.26 years in females. These findings are consistent with studies reporting that SLE typically presents in the third decade of life[1,11]. In our study, the presence of comorbidities and hypertension frequency during follow-up were higher in female patients. It is well known that the prevalence of chronic diseases increases with age[12,13]. Although the age at diagnosis was similar between the groups, the time since diagnosis was significantly longer in females. Additionally, the older age of female patients during the study period may partially explain the higher frequency of comorbidities and hypertension observed in this group.

According to our findings, despite not reaching statistical significance, constitutional symptoms, cutaneous manifestations, and musculoskeletal complaints were most frequently observed as initial complaints in male patients, whereas musculoskeletal complaints and cutaneous manifestations were most common in female patients. Similarly, studies in the literature have reported that weight loss and fever are more frequently observed in male patients[6,14]. In our study, leg swelling as an initial complaint was found to be significantly more frequent in males, which may be due to renal involvement. Indeed, previous studies have reported that renal involvement is more common in male patients, and our findings are consistent with these reports[2,8,15,16].

In our study, consistent with the literature, anti-dsDNA and anti-cardiolipin IgG antibody levels were more frequently elevated in male patients, whereas anti-SS-A antibody positivity was more frequent in females, and complement levels were more frequently decreased in female patients[1,6,8]. In addition, LA positivity was more frequently observed in males compared to females. However, there are also studies

in the literature reporting opposite findings or no significant differences between sexes[8,16,17]. These findings suggest that sex-related differences in the immunological profile of SLE may not be consistent across different patient populations and should therefore be interpreted in the context of population characteristics.

According to our findings, musculoskeletal involvement was the most frequently observed manifestation throughout the disease course in both male and female patients. Consistent with another study in the literature, the frequency of arthralgia was higher than that of arthritis in both sexes[1]. This finding may suggest that more subjective pain-related complaints reported by patients should be carefully considered during the diagnostic evaluation of SLE. In our study, arthritis frequency was similar between male and female patients, whereas mucocutaneous manifestations were more frequently observed in females, although the difference did not reach statistical significance. Additionally, previous studies have also reported that arthritis and cutaneous involvement are less frequent in males compared to females[6,14]. While ocular symptoms were reported to be more frequent in males in the study by Gui et al., sicca symptoms were found to be significantly more frequent in female patients in our study[14]. Renal involvement, consistent with the literature, was significantly higher in male patients compared to females[1,2,8,14,18]. In a meta-analysis by Boodhoo et al., organ involvement such as serositis, pleuritis, and renal involvement was reported to be more frequent in males, whereas arthritis and skin manifestations were more common in females[8]. Furthermore, Albrecht et al. emphasized that male patients are more prone to severe organ-threatening manifestations, such as serositis, lupus nephritis, and neuropsychiatric lupus, and tend to experience greater organ damage[2]. These findings support the concept that male patients with SLE may present with a more severe pattern of organ involvement. Therefore, careful assessment for major organ manifestations, particularly renal involvement, may be warranted during follow-up in male patients.

SLEDAI scores at the last visit were higher in male patients; however, this difference did not reach statistical significance. This finding may be related to the fact that SLEDAI scores were assessed at the final stage of follow-up rather than at disease onset. In the literature, there are studies reporting no significant differences between sexes in terms of SLEDAI scores at disease onset[14], as well as studies reporting significant differences[10,19]. Furthermore, these studies have emphasized that higher SLEDAI scores in male patients may be associated with an increased risk of mortality and complications.

According to our findings, MP IV and CYC IV use was more frequent in male patients. This difference may reflect the higher frequency of renal involvement observed in male patients and is consistent with previous reports in the literature[2,6,10]. These findings further support the importance of careful assessment for organ-threatening manifestations in male patients with SLE, as such manifestations may require more intensive immunosuppressive therapy.

The limitations of our study include its retrospective design, which may have resulted in incomplete access to some patient data from medical records. In addition, the single-center nature of this study and the relatively small sample size may limit the generalizability of the findings. Furthermore, the equalization of male and female patient numbers to improve comparability may have resulted in a sample that does not fully reflect the true sex distribution of the disease, and this should be considered when interpreting the results. In addition, the significantly longer disease duration in female patients may have influenced the cumulative clinical manifestations and treatment exposure observed in this study. Therefore, the observed sex-related differences should be interpreted with caution, as some findings may also have been influenced by these potential confounding factors. The long study period (2010–2025) may have also introduced heterogeneity due to changes in diagnostic criteria, follow-up strategies, and treatment approaches over time. Nevertheless, the fact that our findings are largely consistent with the existing literature supports the internal consistency of our results and strengthens their validity despite the limitations related to sample characteristics.

In conclusion, this study evaluated sex-related differences in the demographic characteristics, antibody profiles, initial complaints, clinical course, and treatment approaches of SLE patients. Our findings indicate that the overall disease course is largely similar between male and female patients. However, renal involvement, one of the potentially life-threatening manifestations, was observed more frequently in males and was associated with more frequent use of aggressive immunosuppressive treatment. This highlights the importance of careful clinical evaluation and close monitoring of renal involvement, particularly in male SLE patients[20]. Nevertheless, the retrospective and single-center design of this study may limit the generalizability of the findings. Thus, further large-scale, prospective, and multicenter studies are needed to better elucidate the impact of sex differences on clinical outcomes in SLE patients.

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