

# Differences between Male and Female Systemic Lupus Erythematosus in a Multiethnic Population

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**ABSTRACT.** *Objective.* Male patients with systemic lupus erythematosus (SLE) are thought to be similar to female patients with SLE, but key clinical characteristics may differ. Comparisons were made between male and female patients with SLE in the Hopkins Lupus Cohort.

*Methods.* A total of 1979 patients in the Hopkins Lupus Cohort were included in the analysis.

*Results.* The cohort consisted of 157 men (66.2% white, 33.8% African American) and 1822 women (59.8% white, 40.2% African American). The mean followup was 6.02 years (range 0–23.73). Men were more likely than women to have disability, hypertension, thrombosis, and renal, hematological, and serological manifestations. Men were more likely to be diagnosed at an older age and to have a lower education level. Women were more likely to have malar rash, photosensitivity, oral ulcers, alopecia, Raynaud's phenomenon, or arthralgia. Men were more likely than women to have experienced end organ damage including neuropsychiatric, renal, cardiovascular, peripheral vascular disease, and myocardial infarction, and to have died. In general, differences between males and females were more numerous and striking in whites, especially with respect to lupus nephritis, abnormal serologies, and thrombosis.

*Conclusion.* Our study suggests that there are major clinical differences between male and female patients with SLE. Differences between male and female patients also depend on ethnicity. Future SLE studies will need to consider both ethnicity and gender to understand these differences. (J Rheumatol First Release March 1 2012; doi:10.3899/jrheum.111061)

## Key Indexing Terms:

SYSTEMIC LUPUS ERYTHEMATOSUS

GENDER

MALE LUPUS

Male lupus is rare, comprising 4%–22% of patients with systemic lupus erythematosus (SLE)<sup>1,2,3,4,5,6,7,8</sup> in different series. Despite numerous studies comparing male and female patients, no consistent differences or characteristics have emerged<sup>9,10</sup>. Male patients had more renal involvement in some, but not all, series<sup>7,11,12,13,14,15,16</sup>. An increased risk of renal failure in males was seen in 2 studies<sup>7,14</sup>. Male patients had more neurological involvement<sup>3,7,9,17</sup>, thrombotic events<sup>9,14,15,17</sup>, cardiovascular damage<sup>14,16,17</sup>, serositis<sup>6,8,11,18</sup>, arthritis<sup>19</sup>, hepatomegaly<sup>19</sup>, low C3<sup>12</sup>, thrombocytopenia<sup>13</sup>, later disease onset<sup>3,20</sup>, fever<sup>12</sup>, infection<sup>17,21</sup>, weight loss<sup>12</sup>, and hypertension<sup>12</sup> in some, but not all, series.

In terms of serology, anticardiolipin antibodies<sup>9,12,14</sup>, anti-dsDNA<sup>15</sup>, and lupus anticoagulant (LAC)<sup>10</sup> were more prevalent in men in a few studies (summarized in Table 1).

There have also been reports of manifestations that occur less often in men, such as skin involvement<sup>6,17,19</sup>, hematological involvement<sup>1,11,21,22</sup>, serological involvement<sup>11,16,21</sup>, Raynaud's phenomenon (RP)<sup>13,15,16,17,19</sup>, and arthritis<sup>6,10,18,21</sup> in some, but not all, series.

The Hopkins Lupus Cohort offered a unique opportunity to compare male versus female SLE, in the largest cohort with systematic followup every 3 months to ensure complete identification of clinical and serologic manifestations. This cohort also offers an opportunity to compare male versus female SLE separately in white and African American patients.

## MATERIALS AND METHODS

*Study population.* The Hopkins Lupus Cohort, established in 1987, comprises patients with SLE receiving ongoing care at the Hopkins Lupus Center. This study has been approved on an annual basis by the Johns Hopkins Hospital Institutional Review Board. Informed written consent is obtained from all subjects. Subjects enrolled in the cohort have clinic visits at 3-month intervals, or more frequently if medically necessary. Ninety-five percent of the patients met the revised American College of Rheumatology (ACR) classification criteria for SLE<sup>23</sup>. The proportions of males to females in the 5% who did not fulfill these criteria were slightly higher than those who did (0.15 vs 0.08). Information recorded at cohort entry (and updated at each visit) consists of basic demographic characteristics (date of birth, age at SLE onset, ethnicity, sex, socioeconomic status, years of education, combined annual household income) and presenting and cumulative clinical manifestations. At each

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Table 1. Studies of male versus female SLE.

Study	No. Male/ Female	Mean Age, yrs	Ethnicity, %	Study Design	Clinical/Laboratory Decreased	SLE Manifestations Increased
Miller 1983 <sup>1</sup>	50/50	45	White 46 AA 2 Asian 2	Cohort	Neurological involvement, alopecia, thrombocytopenia	Pleurisy
Hochberg 1985 <sup>3</sup>	12/138	31.4	White 83 AA 17	Cohort		Later disease onset, peripheral neuropathy
Font 1992 <sup>6</sup>	30/231	34	Spanish	Cohort	Arthritis, malar rash	Discoid lesions, serositis, subacute cutaneous LE
Ward and Studenski 1990 <sup>7</sup>	62/299	44.7	White 64.9	Cross-sectional		Seizures, renal failure
Aydintug 1992 <sup>8</sup>	16/231	ND	United Kingdom	Cohort		Serositis
Cervera 1993 <sup>18</sup>	92/908	37	White 97 AA 2 Other 1	Cohort	Arthritis	Serositis
Koh 1994 <sup>21</sup>	61/86	34.1	Chinese 71 Malay 16 Indian 8 Others 5	Cross-sectional	Arthritis, leukopenia, anti-Ro, anti-La	
Pande 1994 <sup>22</sup>	39/—	ND	Indian	Cross-sectional	Diffuse proliferative lupus nephritis, hypocomplementemia, psychosis	Infections
Specker 1994 <sup>14</sup>	21/82	ND	White	Cross-sectional		Cardiac involvement, renal involvement, endstage renal disease, thromboembolic complications, IgG anticardiolipin
Molina 1996 <sup>15</sup>	107/1209	26	Colombians 49 Mexicans 51	Cross-sectional	Raynaud's	Renal involvement, nephrotic syndrome, vascular thrombosis, anti-dsDNA
Mok 1999 <sup>16</sup>	51/201	31.0	Chinese	Cross-sectional	Alopecia, Raynaud's, anti-Ro	Renal impairment, cardiovascular damage
Keskin 2000 <sup>19</sup>	30/100	36.9	Turkish	Cross-sectional	Alopecia, photosensitivity, skin lesions, Raynaud's	Arthritis, hepatomegaly, pericarditis
Prete 2001 <sup>20</sup>	2188/426	55.5	White 71.2 AA 22.5 Hispanic 4.6 Other 1.7	Retrospective hospital discharge records	Thyroid disease	Older age at onset
Aranow 2002 <sup>9</sup>	18/36	37.3	White 50 AA 17 Hispanic 28 Other 5	Age and duration- matched case-control		Cerebritis, deep venous thrombosis, anticardiolipin
Voulgari 2002 <sup>11</sup>	68/421	43.1	Greek	Cohort	Photosensitivity, mucosal ulcers, anemia, leukopenia, thrombocytopenia, increased ESR, anti-Ro/La	Serositis, renal involvement
Garcia 2005 <sup>12</sup>	123/1091	29.2	White 9.3 AA 10.5 Mestizo 11	Inception cohort	Shorter delay to diagnosis	Fever, weight loss, hypertension, renal disease, hemolytic anemia, IgG anticardiolipin, low C3
Andrade 2007 <sup>10</sup>	63/555	37.1	White 41.3 AA 38.1 Hispanic 18.6	Cohort	Lupus arthritis	LAC, lupus nephritis
Mongkoltanatus 2008 <sup>13</sup>	37/74	34.6	Thai	Age-matched case-control	Alopecia, arthralgia, Raynaud's, psychosis	Thrombocytopenia, renal insufficiency
Stefanidou 2011 <sup>17</sup>	59/535	ND	Greece	Cohort	Arthralgia, alopecia, Raynaud's, photosensitivity	Thromboses, nephropathy, strokes, gastrointestinal tract symptoms, antiphospholipid syndrome, tendonitis, myositis, infections

AA: African American; SLE: systemic lupus erythematosus; LAC: lupus anticoagulant; ND: not determined; ESR: erythrocyte sedimentation rate.

patient visit, disease activity was assessed by the physician's global assessment (0 to 3 on visual analog scale) and the Safety of Estrogens in Lupus Erythematosus National Assessment – Systemic Lupus Erythematosus Disease Activity Index<sup>24</sup>. Laboratory tests included the complete blood cell count, erythrocyte sedimentation rate, serum creatinine, cholesterol, urinalysis, urine protein to creatinine ratio, C3, C4, and anti-dsDNA. The Systemic Lupus International Collaborating Clinics/ACR Damage Index<sup>25</sup> was performed at cohort entry and updated at each visit.

**Patients.** There were 2121 patients in the entire Hopkins Lupus Cohort. We excluded 142 patients who were not white or African American for simplicity. A total of 1799 patients with SLE in the Hopkins Lupus Cohort were included in our analysis. There were 157 men (66.2% whites, 33.8% African Americans, mean age  $49.8 \pm 13.8$  yrs) and 1822 women (59.8% whites, 40.2% African Americans, mean age at entry  $37.6 \pm 12.9$  yrs). Cumulative ACR criteria included 51.4% malar rash, 20.2% discoid rash, 54.3% photosensitivity, 51.4% oral ulcers, 74.1% arthritis, 44.4% pleuritis, 22.5% pericarditis, 41.2% proteinuria, 9.9% seizures, 3.8% psychosis, 10.3% hemolytic anemia, 43.6% leukopenia, 39.6% lymphopenia, 20.2% thrombocytopenia, 62.2% anti-dsDNA, 18.0% anti-Sm, 26.6% LAC, 48.5% anticardiolipin, and 96.5% positive antinuclear antibody. The mean duration of followup in the cohort was 6.02 years (range 0–23.73 yrs). The mean age at last assessment for men was  $47.3 \pm 13.7$  years and for women  $43.7 \pm 13.5$  years. The mean duration of SLE at last assessment for men was  $10.2 \pm 7.6$  years and for women  $11.1 \pm 8.5$  years.

**Statistical analysis.** Male and female patients with SLE were compared with respect to demographic characteristics, clinical manifestations, serologic results, and therapy, using chi-square tests (SAS Institute, Cary, NC, USA). P values were then adjusted for ethnicity, history of smoking, age at last assessment, and duration of SLE at last assessment unless specified. Subsequent analyses focused on African Americans or whites separately and the comparison between African American and white males. A p value  $\leq 0.05$  was considered statistically significant, but OR are presented to allow the reader to assess clinical importance.

## RESULTS

**Clinical and laboratory manifestations in male and female patients.** Demographic, clinical, and laboratory variables are summarized in Table 2. Men were more likely than women to have disability, lymphopenia, thrombocytopenia, positive anti-Sm, direct Coombs test, LAC, low C3, and anti-dsDNA. Men were also more likely to have had renal involvement, thrombotic events, and hypertension, compared to women. Men were more likely to be diagnosed at an older age and to have a lower education level than women. Men were less likely to have had malar rash, photosensitivity, oral ulcer, alopecia, RP, and arthralgias than women.

**Damage in male and female patients.** Organ damage is summarized in Table 3 using the variables of the SLICC/ACR Damage Index. Men were more likely than women to have had neuropsychiatric, renal or cardiovascular manifestations, peripheral vascular disease, and myocardial infarction (MI), and to have died.

**Gender differences by ethnicity.** Table 4 summarizes comparisons in the African American subset ( $n = 785$ ). African American men were more likely to have had disability, history of smoking, proteinuria, and renal insufficiency than African American women. African American men were more likely to be diagnosed at an older age. They were also more likely than African American women to have neuropsychi-

atric, renal, and cardiovascular damage or to have died. However, they were less likely to have had alopecia.

Comparisons of white patients are shown in Table 5. White males were more likely than white women to have had obesity, disability, thrombocytopenia, a positive Coombs test, LAC, anti-Sm, anti-dsDNA, low C3, hypertension, and deep vein thrombosis. White men were also more likely to be diagnosed at an older age. In addition, they also had more renal manifestations such as proteinuria, nephrotic syndrome, hematuria, renal insufficiency, renal failure, and abnormal renal biopsy. They were more likely to experience neuropsychiatric, renal, cardiovascular, and musculoskeletal damage than white women. Endstage renal disease occurred in 6.7% of white men compared to 2.6% of white women (adjusted p value = 0.0141). White men were less likely than white women to have had malar rash, photosensitivity, oral ulcers, alopecia, or RP.

To further investigate the differences related to ethnicity, a comparison between white and African American males was performed (Table 6). African American men were more likely to have had discoid rash, alopecia, renal involvement such as proteinuria and renal insufficiency, and anti-Sm than white men. They were more likely to have later onset of lupus and to have a lower education level. However, they were less likely to have LAC. In addition, African American men were more likely than white men to have renal, pulmonary, and cardiovascular damage, and to have died.

## DISCUSSION

Male lupus has been thought to be clinically similar to female lupus<sup>7</sup>. Studies have reached conflicting results (Table 1), although several found arthritis to be less common in men with SLE. Several studies have found more organ damage in men, in particular renal insufficiency/failure. Our study has the largest number of men (except for the Veterans Administration study<sup>20</sup>, which did not systematically examine disease manifestations) and the largest prospective followup. In addition, the ethnic makeup of the Hopkins Lupus Cohort allowed us to look separately at white and African American male SLE.

We observed differences between men and women with respect to a large number of disease manifestations and outcomes. Among the differences found in our study, some dermatologic features such as oral ulcer and alopecia, some serologic tests such as LAC, and the renal manifestations such as renal insufficiency and renal failure, had OR  $> 2.0$  or  $< 0.5$ , suggesting differences of substantial clinical importance.

In the all-patient analyses (Table 2), men were more likely than women to have had lymphopenia, thrombocytopenia, direct Coombs, LAC, anti-Sm, low C3, and anti-dsDNA. The striking increase in manifestations of hematologic and serologic lupus was suggested in one previous study that found an increase in thrombocytopenia<sup>13</sup>, one that found an increase in hemolytic anemia and low C3<sup>12</sup>, and one that found an

Table 2. Comparison of cumulative clinical and laboratory features between male and female SLE (n = 1979).

Characteristics/manifestations	Male, n = 157 n (%)	Female, n = 1822 n (%)	OR (95% CI)*	Adjusted p*
Ethnic group				
African American	53 (33.8)	732 (40.2)	1.3 (0.9, 1.9)**	0.1276***
White	104 (66.2)	1090 (59.8)		
Age at last assessment, yrs				
≤ 30	20 (13.0)	331 (18.4)	1.5 (0.9, 2.5)**	0.1229†
> 30	134 (87.0)	1470 (81.6)		
Age at onset, yrs				
≤ 30	67 (43.2)	1093 (60.7)	1.2 (0.7, 2.1)**	0.6047
> 30	88 (56.8)	708 (39.3)		
Age at diagnosis, yrs				
≤ 30	51 (32.7)	928 (51.1)	1.9 (1.2, 3.1)**	0.0056††
> 30	105 (67.3)	887 (48.9)		
Education level, yrs				
≤ 12	68 (46.6)	627 (36.2)	1.5 (1.1, 2.2)**	0.0218
> 12	78 (53.4)	1105 (63.8)		
Annual income				
≤ \$50,000	76 (55.9)	955 (59.7)	1.1 (0.7, 1.6)**	0.7108
> \$50,000	60 (44.1)	646 (40.4)		
Disability	51 (32.9)	394 (22.2)	1.8 (1.2, 2.6)	0.0022
Family history	34 (21.7)	491 (27.1)	0.8 (0.5, 1.1)	0.1680
History of smoking	76 (48.7)	701 (38.6)	1.3 (1.0, 1.9)	0.0911
Clinical features				
Malar rash	62 (39.7)	953 (52.4)	0.6 (0.4, 0.9)	0.0109
Discoid rash	38 (24.7)	360 (19.8)	1.4 (0.9, 2.1)	0.1336
Photosensitivity	63 (40.4)	1007 (55.5)	0.5 (0.4, 0.7)	0.0002
Oral ulcer	53 (34.0)	961 (52.9)	0.4 (0.3, 0.6)	< 0.0001
Alopecia	44 (28.2)	1023 (56.3)	0.3 (0.2, 0.4)	< 0.0001
RP	56 (35.7)	987 (54.4)	0.5 (0.3, 0.7)	< 0.0001
Subacute cutaneous lupus	11 (7.1)	93 (5.1)	1.2 (0.6, 2.3)	0.6092
Bullous lupus	2 (1.3)	13 (0.7)	1.9 (0.4, 8.6)	0.4248
Vasculitis (cutaneous)	19 (12.3)	270 (14.9)	0.9 (0.5, 1.5)	0.6903
Arthralgias	137 (87.3)	1688 (92.7)	0.5 (0.3, 0.9)	0.0188
Arthritis	109 (70.3)	1347 (74.4)	0.8 (0.6, 1.2)	0.3267
Pleuritis	65 (41.7)	810 (44.7)	0.9 (0.6, 1.3)	0.5262
Pericarditis	39 (25.0)	403 (22.3)	1.3 (0.9, 1.9)	0.1965
Proteinuria	78 (50.0)	732 (40.4)	1.9 (1.3, 2.8)	0.0003
Nephrotic syndrome	36 (23.8)	299 (16.6)	2.0 (1.3, 3.1)	0.0010
Hematuria	54 (34.8)	492 (27.2)	1.7 (1.2, 2.5)	0.0028
Renal insufficiency	49 (34.1)	343 (18.9)	2.2 (1.5, 3.2)	< 0.0001
Renal failure	24 (15.3)	138 (7.6)	2.7 (1.6, 4.4)	0.0002
Renal biopsy	56 (35.7)	470 (25.8)	2.0 (1.4, 2.9)	0.0002
Hemolytic anemia	19 (12.8)	178 (10.1)	1.4 (0.8, 2.4)	0.1951
Leukopenia	74 (47.4)	785 (43.3)	1.3 (0.9, 1.9)	0.1055
Lymphopenia	77 (49.4)	698 (38.8)	1.5 (1.1, 2.1)	0.0179
Thrombocytopenia	45 (28.8)	353 (19.5)	1.9 (1.3, 2.7)	0.0013
Seizures	20 (12.7)	175 (9.6)	1.5 (0.9, 2.4)	0.1247
Psychosis	7 (4.5)	67 (3.7)	1.3 (0.6, 2.9)	0.5036
Laboratory findings				
Coombs positivity	35 (26.9)	281 (19.6)	1.7 (1.1, 2.6)	0.0133
Lupus anticoagulant	62 (41.3)	446 (25.3)	2.1 (1.5, 2.9)	< 0.0001
Anti-Sm	36 (23.5)	308 (17.5)	1.8 (1.2, 2.7)	0.0061
Anti-dsDNA	107 (68.2)	1120 (61.7)	1.5 (1.1, 2.2)	0.0229
Anti-Ro	37 (23.9)	526 (29.9)	0.8 (0.5, 1.1)	0.1795
Anti-La	12 (7.7)	229 (13.0)	0.6 (0.3, 1.1)	0.0783
Anticardiolipin	76 (51.4)	849 (48.3)	1.1 (0.8, 1.6)	0.4350
β <sub>2</sub> -glycoprotein	31 (36.0)	291 (30.0)	1.4 (0.9, 2.2)	0.1658
Anti-RNP	46 (29.7)	462 (26.4)	1.4 (0.9, 2.1)	0.0965
Low C3	94 (60.3)	967 (53.2)	1.6 (1.1, 2.3)	0.0071
Low C4	74 (47.4)	851 (46.9)	1.2 (0.8, 1.6)	0.3930
Increased ESR	120 (77.9)	1350 (74.8)	1.4 (0.9, 2.1)	0.1102

Table 2. Continued.

Characteristics/manifestations	Male, n = 157 n (%)	Female, n = 1822 n (%)	OR (95% CI)*	Adjusted p*
History of hypertension	103 (65.6)	944 (51.9)	1.8 (1.2, 2.6)	0.0019
Hypercholesterolemia	96 (61.9)	1002 (55.4)	1.2 (0.9, 1.8)	0.2408
Obesity	82 (53.2)	879 (48.6)	1.2 (0.8, 1.7)	0.3227
Deep vein thrombosis	31 (19.9)	242 (13.3)	1.7 (1.1, 2.7)	0.0103

\* Adjusted for ethnicity, history of smoking, age at last assessment, and duration of SLE at last assessment unless specified. \*\* The ratio of the odds of the event “white,” “> 30,” “≤ 12,” or “> \$50,000” occurring in males to the odds in females. \*\*\* Adjusted for history of smoking, age at last assessment, and duration of SLE at last assessment. † Adjusted for ethnicity, history of smoking, and duration of SLE at last assessment. †† Adjusted for ethnicity, history of smoking, and age at last assessment. SLE: systemic lupus erythematosus; RP: Raynaud’s phenomenon; ESR: erythrocyte sedimentation rate.

increase in anti-dsDNA<sup>15</sup>. The increase in LAC was reported in only one previous study<sup>10</sup>, but 3 studies found an increase in anticardiolipin<sup>9,12,14</sup>.

Men were more likely to have had an MI. This may be partially explained by the increase in several risk factors, including hypertension and LAC. In contrast, men were less likely to have dermatologic manifestations, including malar rash, photosensitive rash, oral ulcers, alopecia, and RP. A decreased frequency of RP has been found in 3 previous studies<sup>13,16,17</sup>. A decrease in alopecia was reported in 3 previous studies<sup>13,16,17</sup>. Our study differs strikingly from several others<sup>10,18,21</sup> that found less arthritis in male SLE: there was no difference at all in our analysis. But our results agreed with 2 recent studies<sup>13,17</sup> that found less arthralgia in male SLE.

We next analyzed white and African American lupus separately and did a direct comparison between African American and white men. African American men (compared to African American women) were more likely to have a history of smoking and less likely to have alopecia. African American men had a major increase in renal impairment and in death, compared to African American women. White men had less malar rash, photosensitivity, oral ulcers, alopecia, and RP than white women. They had more direct Coombs, thrombocytopenia, and LAC, and more obesity and hypertension than white women. African American men had more dermatologic lupus and more organ damage, including renal, pulmonary, and cardiovascular damage, than white men.

Strikingly, all damage differences except hypertension between male and female patients, and proteinuria between African American male and female patients, achieved an OR > 2.0, which strongly indicated that male patients with SLE had much more severe organ damage than female patients with SLE.

The substantial gender difference in disease manifestations is likely not just due to differences in estrogen or testosterone levels. Lu, *et al*<sup>26</sup> reviewed a number of hypotheses to explain the underlying mechanism of gender differences, including the sex hormone hypothesis, the sex chromosome hypothesis, and the intrauterine selection hypothesis. In mice, Y chromosome polymorphism, X chromosome inactivation, X chromo-

some gene dosage and parental imprint can all affect autoimmunity<sup>27,28,29,30,31,32</sup>. Although SLE was found to be of greater severity in female than in male mice<sup>33</sup>, many studies, including our own, suggest the opposite is true for many organ manifestations in humans. Another possible explanation for some gender differences is that male patients are less likely to seek medical assistance, which might lead to later presentation, with more clinical manifestations, and lead to more organ damage and mortality. This might be part of the reason why, in our study, men tended to have later onset of SLE and diagnosis. Nevertheless, it remains unknown why male SLE differs substantially from female SLE and has a more severe expression in some organs.

There are major clinical differences between male and female lupus: more renal and hematologic lupus in males and less dermatologic lupus in males. Some of these differences, such as more proteinuria and hematuria, are found only in white patients. Men, regardless of ethnicity, had more renal insufficiency. Ethnicity greatly affected the results. White men had more MI than white women, but African American men did not have more MI than African American women. Studies of SLE are needed to analyze not just ethnicity but also gender, to further understand these differences and their underlying mechanisms.

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Table 3. SLICC/ACR Damage Index comparison between male and female SLE (n = 1979).

Damage	Male, n = 157 n (%)	Female, n = 1822 n (%)	OR (95% CI)*	Adjusted p*
Ocular				
Any cataract ever	23 (15.0)	289 (16.6)	0.8 (0.5, 1.3)	0.2895
Retinal change or optic atrophy	11 (7.1)	82 (4.6)	1.3 (0.7, 2.6)	0.4503
Neuropsychiatric				
Cognitive impairment	17 (11.0)	129 (7.2)	1.4 (0.8, 2.5)	0.2245
Seizures requiring therapy for 6 mo	4 (9.0)	81 (4.5)	2.3 (1.2, 4.1)	0.0076
Cerebral vascular accident ever	14 (9.0)	160 (8.9)	0.9 (0.5, 1.7)	0.8519
Cranial or peripheral neuropathy	15 (9.7)	180 (10.0)	0.9 (0.5, 1.6)	0.6940
Transverse myelitis	0 (0.0)	17 (1.0)	—	Too few
Renal				
GFR < 50%	21 (13.5)	105 (5.8)	2.9 (1.7, 4.9)	0.0001
Proteinuria > 3.5 g/day	22 (14.3)	130 (7.2)	2.6 (1.5, 4.5)	0.0005
Endstage renal disease	13 (8.4)	85 (4.7)	2.3 (1.2, 4.5)	0.0102
Pulmonary				
Pulmonary hypertension	8 (5.2)	87 (4.8)	0.9 (0.4, 2.0)	0.7657
Pulmonary fibrosis	10 (6.5)	126 (7.0)	0.9 (0.4, 1.7)	0.6640
Shrinking lung	0 (0.0)	7 (0.4)	—	Too few
Pleural fibrosis	5 (3.2)	48 (2.7)	—	Too few
Pulmonary infarction	1 (0.6)	10 (0.6)	—	Too few
Cardiovascular				
Angina	12 (7.7)	56 (3.1)	2.2 (1.1, 4.3)	0.0277
Myocardial infarction	17 (11.0)	68 (3.8)	2.5 (1.3, 4.8)	0.0040
Cardiomyopathy	10 (6.5)	67 (3.7)	1.5 (0.7, 3.2)	0.3404
Valvular disease	2 (1.3)	50 (2.8)	—	Too few
Pericarditis	1 (0.6)	36 (2.0)	—	Too few
Left ventricular hypertrophy	18 (11.8)	106 (6.1)	2.3 (1.3, 4.0)	0.0042
Hypertension for > 6 mo	69 (45.4)	614 (34.3)	1.6 (1.1, 2.2)	0.0151
Peripheral vascular				
Venous thrombosis	14 (9.0)	65 (3.6)	2.9 (1.6, 5.4)	0.0006
Claudication for > 6 mo	3 (1.9)	27 (1.5)	—	Too few
Minor tissue loss	2 (1.3)	14 (0.8)	—	Too few
Significant tissue loss	1 (0.6)	20 (1.1)	—	Too few
Gastrointestinal (GI)				
Infarction or resection of bowel	20 (12.9)	261 (14.5)	0.8 (0.5, 1.3)	0.3232
Mesenteric insufficiency	0 (0.0)	9 (0.5)	—	Too few
Chronic peritonitis	0 (0.0)	8 (0.4)	—	Too few
Upper GI stricture or surgery	2 (1.3)	20 (1.1)	—	Too few
Pancreatitis	1 (0.6)	11 (0.6)	—	Too few
Musculoskeletal				
Muscle atrophy or weakness	3 (1.9)	59 (3.3)	0.6 (0.2, 1.9)	0.3577
Deforming or erosive arthritis	6 (3.8)	124 (7.0)	0.6 (0.2, 1.3)	0.1957
Osteoporosis	14 (9.0)	218 (12.0)	0.7 (0.4, 1.2)	0.1747
Avascular necrosis	18 (11.5)	177 (9.8)	1.6 (0.9, 2.8)	0.0845
Osteomyelitis	3 (1.9)	17 (0.9)	—	Too few
Ruptured tendon	3 (1.9)	51 (2.8)	—	Too few
Skin				
Scarring chronic alopecia	5 (3.2)	81 (4.5)	—	Too few
Extensive scarring or panniculum	2 (1.3)	52 (2.9)	—	Too few
Skin ulceration for > 6 mo	3 (1.9)	25 (1.4)	—	Too few
Endocrine				
Premature gonadal failure	1 (0.6)	100 (5.6)	—	Too few
Diabetes	16 (10.3)	153 (8.5)	1.1 (0.7, 2.0)	0.6351
Malignancy	24 (15.7)	178 (9.9)	1.6 (1.0, 2.6)	0.0613
Death	18 (11.5)	113 (6.2)	2.0 (1.1, 3.4)	0.0159

\* Adjusted for ethnicity, history of smoking, age at last assessment, and duration of SLE at last assessment. GFR: glomerular filtration rate; SLICC/ACR: Systemic Lupus International Collaborating Clinics/American College of Rheumatology; SLE: systemic lupus erythematosus.

Table 4. Comparison of male and female African American SLE (n = 785).

Characteristics/manifestations	Male, n = 53 n (%)	Female, n = 732 n (%)	OR (95% CI)*	Adjusted p*
Cumulative clinical and laboratory features				
Age at last assessment, yrs				
≤ 30	7 (14.0)	138 (19.1)	1.3 (0.6, 3.1)**	0.5202†
> 30	43 (86.0)	586 (80.9)		
Age at onset, yrs				
≤ 30	18 (34.6)	436 (60.0)	1.7 (0.5, 5.6)**	0.4145
> 30	34 (65.4)	291 (40.0)		
Age at diagnosis, yrs				
≤ 30	17 (32.1)	387 (53.0)	2.2 (1.0, 4.9)**	0.0481††
> 30	36 (67.9)	343 (47.0)		
Education level, yrs				
≤ 12	28 (62.2)	313 (44.9)	1.8 (1.0, 3.5)**	0.0705
> 12	17 (37.8)	384 (55.1)		
Obesity	23 (46.0)	420 (58.0)	0.6 (0.3, 1.1)	0.0749
Disability	22 (43.1)	197 (27.6)	1.9 (1.0, 3.5)	0.0395
History of smoking	31 (58.5)	279 (38.2)	2.0 (1.1, 3.6)	0.0327
Clinical features				
Malar rash	16 (30.2)	325 (44.4)	0.7 (0.4, 1.2)	0.2041
Discoid rash	23 (45.1)	219 (30.0)	1.6 (0.9, 3.1)	0.1186
Photosensitivity	20 (37.7)	306 (41.9)	1.0 (0.5, 1.8)	0.9696
Oral ulcer	17 (32.1)	304 (41.5)	0.7 (0.4, 1.3)	0.2687
Alopecia	24 (45.3)	521 (71.3)	0.3 (0.2, 0.5)	< 0.0001
RP	20 (37.7)	361 (49.4)	0.7 (0.4, 1.3)	0.2722
Arthralgias	46 (86.8)	690 (94.3)	0.4 (0.2, 1.1)	0.0698
Arthritis	38 (73.1)	572 (78.6)	0.8 (0.4, 1.6)	0.5264
Proteinuria	34 (65.4)	403 (55.4)	1.9 (1.0, 3.6)	0.0450
Nephrotic syndrome	13 (26.0)	194 (26.9)	1.0 (0.5, 2.1)	0.9531
Hematuria	21 (40.4)	265 (36.5)	1.4 (0.8, 2.6)	0.2431
Renal insufficiency	24 (46.2)	187 (25.7)	2.7 (1.5, 5.0)	0.0012
Renal failure	11 (20.8)	86 (11.8)	2.1 (1.0, 4.7)	0.0599
Renal biopsy	23 (43.4)	268 (36.6)	1.5 (0.8, 2.7)	0.2176
Lymphopenia	28 (53.9)	287 (39.4)	1.6 (0.9, 2.8)	0.1295
Thrombocytopenia	16 (30.8)	161 (22.0)	1.5 (0.8, 3.0)	0.1982
Laboratory findings				
Coombs positivity	13 (29.6)	158 (26.0)	1.1 (0.5, 2.2)	0.8299
Lupus anticoagulant	13 (27.7)	166 (23.5)	1.2 (0.6, 2.4)	0.5978
Anti-Sm	17 (33.3)	197 (27.6)	1.4 (0.7, 2.6)	0.3096
Anti-dsDNA	34 (64.2)	485 (66.3)	1.1 (0.6, 2.0)	0.8506
Low C3	31 (59.6)	432 (59.0)	1.2 (0.6, 2.1)	0.5971
Low C4	22 (42.3)	358 (49.0)	0.8 (0.5, 1.5)	0.5215
History of hypertension	39 (73.6)	472 (64.5)	1.3 (0.7, 2.7)	0.4119
Deep vein thrombosis	8 (15.4)	97 (13.3)	1.4 (0.6, 3.1)	0.4043
SLICC/ACR Damage Index				
Neuropsychiatric damage				
Cognitive impairment	8 (15.7)	42 (5.8)	2.7 (1.1, 6.7)	0.0282
Seizures requiring therapy for 6 mo	4 (7.8)	31 (4.3)	2.4 (0.8, 7.3)	0.1212
Renal damage				
GFR < 50%	12 (23.5)	62 (8.6)	3.1 (1.4, 6.6)	0.0039
Proteinuria 3.5 g/24 h	8 (15.7)	88 (12.2)	1.4 (0.6, 3.5)	0.4906
Endstage renal disease	6 (11.8)	57 (7.9)	1.8 (0.7, 4.9)	0.2441
Pulmonary damage				
Pulmonary fibrosis	7 (13.7)	68 (9.4)	1.5 (0.6, 3.6)	0.4199
Cardiovascular damage				
Angina	2 (3.9)	20 (2.8)	1.1 (0.2, 5.3)	0.8679
Myocardial infarction	6 (11.8)	32 (4.4)	1.7 (0.5, 5.2)	0.3745
Cardiomyopathy	7 (13.7)	42 (5.8)	1.7 (0.6, 4.6)	0.3011
Left ventricular hypertrophy	9 (18.0)	74 (10.5)	2.0 (0.9, 4.5)	0.0908
Venous thrombosis	3 (5.9)	23 (3.2)	2.3 (0.7, 8.2)	0.1913
Hypertension for > 6 mo	34 (69.4)	315 (43.8)	2.4 (1.3, 4.7)	0.0085

Table 4. Continued.

Characteristics/manifestations	Male, n = 53 n (%)	Female, n = 732 n (%)	OR (95% CI)*	Adjusted p*
Musculoskeletal				
Avascular necrosis	6 (11.5)	112 (15.4)	1.0 (0.4, 2.4)	0.9397
Malignancy	6 (12.0)	63 (8.7)	1.4 (0.6, 3.5)	0.4783
Death	12 (22.6)	65 (8.9)	2.8 (1.4, 5.8)	0.0042

\* Adjusted for ethnicity, history of smoking, age at last assessment, and duration of SLE at last assessment.

\*\* The ratio of the odds of the event "> 30," or "≤ 12," occurring in males to the odds in females. † Adjusted for ethnicity, history of smoking, and duration of SLE at last assessment. †† Adjusted for ethnicity, history of smoking, and age at last assessment. GFR: glomerular filtration rate; SLE: systemic lupus erythematosus; RP: Raynaud's phenomenon; SLICC/ACR: Systemic Lupus International Collaborating Clinics/American College of Rheumatology.

Table 5. Comparison of male and female white SLE (n = 1194).

Characteristics/manifestations	Male, n = 104 n (%)	Female, n = 1090 n (%)	OR (95% CI)*	Adjusted p*
Cumulative clinical and laboratory features				
Age at last assessment, yrs				
≤ 30	13 (12.5)	193 (17.9)	1.5 (0.8, 2.9)**	0.1770†
> 30	91 (87.5)	884 (82.1)		
Age at onset, yrs				
≤ 30	49 (47.6)	657 (61.2)	1.1 (0.6, 2.1)**	0.8492
> 30	54 (52.4)	417 (38.8)		
Age at diagnosis, yrs				
≤ 30	34 (33.0)	541 (49.9)	1.8 (1.0, 3.3)**	0.0394††
> 30	69 (67.0)	544 (50.1)		
Education level, yrs				
≤ 12	40 (39.6)	314 (69.7)	1.4 (0.9, 2.2)**	0.1264
> 12	61 (60.4)	721 (60.4)		
Obesity	59 (56.7)	459 (42.4)	1.7 (1.1, 2.5)	0.0155
Disability	29 (27.9)	197 (18.5)	1.7 (1.1, 2.7)	0.0254
History of smoking	45 (43.7)	422 (38.9)	1.1 (0.7, 1.7)	0.5589
Clinical features				
Malar rash	46 (44.7)	628 (57.8)	0.6 (0.4, 0.9)	0.0227
Discoid rash	15 (14.6)	141 (13.0)	1.2 (0.6, 2.1)	0.6149
Photosensitivity	43 (41.8)	701 (64.7)	0.4 (0.3, 0.6)	< 0.0001
Oral ulcer	36 (35.0)	657 (60.5)	0.4 (0.2, 0.6)	< 0.0001
Alopecia	20 (19.4)	502 (46.3)	0.3 (0.2, 0.5)	< 0.0001
RP	36 (34.6)	626 (57.7)	0.4 (0.3, 0.6)	< 0.0001
Arthralgias	91 (87.5)	998 (91.7)	0.6 (0.3, 1.1)	0.1051
Arthritis	71 (68.9)	775 (71.6)	0.8 (0.5, 1.3)	0.4554
Proteinuria	44 (42.3)	329 (30.4)	1.9 (1.3, 3.0)	0.0027
Nephrotic syndrome	23 (22.8)	105 (9.8)	3.2 (1.9, 5.5)	< 0.0001
Hematuria	33 (32.0)	227 (20.9)	2.0 (1.2, 3.0)	0.0033
Renal insufficiency	25 (24.0)	156 (14.4)	2.0 (1.2, 3.2)	0.0071
Renal failure	13 (12.5)	52 (4.8)	3.2 (1.6, 6.2)	0.0006
Renal biopsy	33 (31.7)	202 (18.5)	2.4 (1.5, 3.8)	0.0002
Lymphopenia	49 (47.1)	411 (38.4)	1.4 (1.0, 2.2)	0.0805
Thrombocytopenia	29 (27.9)	192 (17.7)	2.0 (1.3, 3.3)	0.0029
Laboratory findings				
Coombs positivity	22 (25.6)	123 (14.8)	2.3 (1.3, 3.9)	0.0030
Lupus anticoagulant	49 (47.6)	280 (26.5)	2.6 (1.7, 3.9)	< 0.0001
Anti-Sm	19 (18.6)	111 (10.6)	2.2 (1.2, 3.7)	0.0059
Anti-dsDNA	73 (70.2)	635 (58.6)	1.9 (1.2, 2.9)	0.0073
Low C3	63 (60.6)	535 (49.3)	1.9 (1.2, 2.9)	0.0041
Low C4	52 (50.0)	493 (45.5)	1.4 (0.9, 2.1)	0.1371
History of hypertension	64 (61.5)	472 (43.5)	2.0 (1.3, 3.1)	0.0020
Deep vein thrombosis	23 (22.1)	145 (13.4)	1.9 (1.2, 3.2)	0.0110



Table 5. Continued.

Characteristics/manifestations	Male, n = 104 n (%)	Female, n = 1090 n (%)	OR (95% CI)*	Adjusted p*
SLICC/ACR Damage Index				
Neuropsychiatric damage				
Cognitive impairment	9 (8.7)	87 (8.1)	1.0 (0.5, 2.1)	0.9535
Seizures requiring therapy for 6 mo	10 (9.6)	50 (4.6)	2.3 (1.1, 4.7)	0.0233
Renal damage				
GFR < 50%	9 (8.7)	43 (4.0)	2.6 (1.2, 5.5)	0.0158
Proteinuria 3.5 g/24 h	14 (13.6)	42 (3.9)	4.2 (2.1, 8.2)	< 0.0001
Endstage renal disease	7 (6.7)	28 (2.6)	3.0 (1.2, 7.1)	0.0141
Pulmonary damage				
Pulmonary fibrosis	3 (2.9)	58 (5.4)	0.5 (0.1, 1.6)	0.2214
Cardiovascular damage				
Angina	10 (9.6)	36 (3.3)	2.7 (1.2, 6.0)	0.0133
Myocardial infarction	11 (10.6)	36 (3.3)	3.2 (1.5, 7.1)	0.0033
Cardiomyopathy	3 (2.9)	25 (2.3)	1.2 (0.3, 4.1)	0.7813
Left ventricular hypertrophy	9 (8.7)	32 (3.1)	2.7 (1.2, 6.0)	0.0157
Venous thrombosis	11 (10.6)	42 (3.9)	3.2 (1.6, 6.5)	0.0014
Hypertension for > 6 mo	35 (34)	299 (27.9)	1.3 (0.8, 2.0)	0.3125
Musculoskeletal				
Avascular necrosis	12 (11.5)	65 (6.0)	2.3 (1.2, 4.5)	0.0144
Malignancy	18 (17.5)	115 (10.7)	1.7 (0.9, 3.0)	0.0773
Death	6 (5.8)	48 (4.4)	1.2 (0.5, 3.0)	0.6302

\* Adjusted for ethnicity, history of smoking, age at last assessment, and duration of SLE at last assessment.

\*\* The ratio of the odds of the event "> 30," or "≤ 12," occurring in males to the odds in females. † Adjusted for ethnicity, history of smoking, and duration of SLE at last assessment. †† Adjusted for ethnicity, history of smoking, and age at last assessment. SLE: systemic lupus erythematosus; RP: Raynaud's phenomenon; SLICC/ACR: Systemic Lupus International Collaborating Clinics/American College of Rheumatology; GFR: glomerular filtration rate.

Table 6. Comparison of African American (AA) and white male SLE (n = 157).

Characteristics/manifestations	AA, n = 53 n (%)	White, n = 104 n (%)	OR (95% CI)*	Adjusted p*
Cumulative clinical and laboratory features				
Age at last assessment, yrs				
≤ 30	7 (14.0)	13 (12.5)	0.9 (0.3, 2.5)**	0.8237 <sup>†</sup>
> 30	43 (86.0)	91 (87.5)		
Age at onset, yrs				
≤ 30	18 (34.6)	49 (47.6)	3.1 (1.0, 9.4)**	0.0477
> 30	34 (65.4)	54 (52.4)		
Age at diagnosis, yrs				
≤ 30	17 (32.1)	34 (33.0)	1.1 (0.4, 3.4)**	0.8210 <sup>††</sup>
> 30	36 (67.9)	69 (67.0)		
Education level, yrs				
≤ 12	28 (62.2)	40 (39.6)	2.4 (1.1, 5.0)**	0.0199
> 12	17 (37.8)	61 (60.4)		
Obesity	23 (46.0)	59 (56.7)	0.7 (0.3, 1.4)	0.3204
Disability	22 (43.1)	29 (27.9)	2.0 (0.9, 4.0)	0.0727
History of smoking	31 (58.5)	45 (43.7)	1.9 (0.9, 3.8)	0.0903
Clinical features				
Malar rash	16 (30.2)	46 (44.7)	0.5 (0.3, 1.1)	0.0860
Discoid rash	23 (45.1)	15 (14.6)	4.3 (1.9, 9.5)	0.0004
Photosensitivity	20 (37.7)	43 (41.8)	0.8 (0.4, 1.7)	0.5784
Oral ulcer	17 (32.1)	36 (34.9)	0.9 (0.4, 1.8)	0.6766
Alopecia	24 (45.3)	20 (19.4)	3.0 (1.4, 6.4)	0.0043
RP	20 (37.7)	36 (34.6)	1.1 (0.5, 2.2)	0.8370
Arthralgias	46 (86.8)	91 (87.5)	1.0 (0.3, 3.2)	0.9480

Table 6. Continued.

Characteristics/manifestations	AA, n = 53 n (%)	White, n = 104 n (%)	OR (95% CI)*	Adjusted p*
Arthritis	38 (73.1)	71 (68.9)	1.5 (0.7, 3.4)	0.2980
Proteinuria	34 (65.4)	44 (42.3)	2.8 (1.3, 5.9)	0.0071
Nephrotic syndrome	13 (26.0)	23 (22.8)	1.0 (0.5, 2.4)	0.9234
Hematuria	21 (40.4)	33 (32.0)	1.3 (0.6, 2.7)	0.4556
Renal insufficiency	24 (46.2)	25 (24.0)	2.7 (1.3, 5.6)	0.0104
Renal failure	11 (20.8)	13 (12.5)	1.6 (0.6, 4.1)	0.3594
Renal biopsy	23 (43.4)	33 (31.7)	1.6 (0.7, 3.4)	0.2307
Lymphopenia	28 (53.9)	49 (47.1)	1.3 (0.6, 2.6)	0.4902
Thrombocytopenia	16 (30.8)	29 (27.9)	1.0 (0.5, 2.2)	0.9954
Laboratory findings				
Coombs positivity	13 (29.6)	22 (25.6)	1.0 (0.4, 2.5)	0.9557
Lupus anticoagulant	13 (27.7)	49 (47.6)	0.4 (0.2, 0.8)	0.0183
Anti-Sm	17 (33.3)	19 (18.6)	2.6 (1.1, 6.0)	0.0247
Anti-dsDNA	34 (64.2)	73 (70.2)	0.7 (0.4, 1.6)	0.4479
Low C3	31 (59.6)	63 (60.6)	0.9 (0.4, 1.7)	0.6296
Low C4	22 (42.3)	52 (50.0)	0.6 (0.3, 1.3)	0.2434
History of hypertension	39 (73.6)	64 (61.5)	1.9 (0.9, 4.1)	0.1010
Deep vein thrombosis	8 (15.4)	23 (22.1)	0.7 (0.3, 1.7)	0.4188
SLICC/ACR Damage Index				
Neuropsychiatric damage				
Cognitive impairment	8 (15.7)	9 (8.7)	2.1 (0.7, 6.3)	0.1802
Seizures requiring therapy for 6 mo	4 (7.8)	10 (9.6)	0.8 (0.2, 2.9)	0.7546
Renal damage				
GFR < 50%	12 (23.5)	9 (8.7)	3.1 (1.1, 8.8)	0.0309
Proteinuria 3.5 g/24 h	8 (15.7)	14 (13.6)	1.0 (0.4, 3.0)	0.9424
Endstage renal disease	6 (11.8)	7 (6.7)	1.8 (0.5, 6.1)	0.3700
Pulmonary damage				
Pulmonary fibrosis	7 (13.7)	3 (2.9)	4.8 (1.0, 21.9)	0.0452
Cardiovascular damage				
Angina	2 (3.9)	10 (9.6)	0.3 (0.1, 1.8)	0.1985
Myocardial infarction	6 (11.8)	11 (10.6)	0.7 (0.2, 2.5)	0.5883
Cardiomyopathy	7 (13.7)	3 (2.9)	4.0 (0.9, 17.8)	0.0707
Left ventricular hypertrophy	9 (18.0)	9 (8.7)	2.7 (0.9, 7.8)	0.0667
Venous thrombosis	3 (5.9)	11 (10.6)	0.6 (0.2, 2.3)	0.4651
Hypertension for > 6 mo	34 (69.4)	35 (34.0)	3.8 (1.8, 8.1)	0.0004
Musculoskeletal damage				
Avascular necrosis	6 (11.5)	12 (11.5)	1.0 (0.3, 3.0)	0.9695
Malignancy	6 (12.0)	18 (17.5)	0.6 (0.2, 1.7)	0.3651
Death	12 (22.6)	6 (5.8)	4.4 (1.1, 16.9)	0.0333

\* Adjusted for history of smoking, age at last assessment, and duration of SLE at last assessment. \*\* The ratio of the odds of the event "> 30," or "< 12," occurring in males to the odds in females. † Adjusted for ethnicity, history of smoking, and duration of SLE at last assessment. †† Adjusted for ethnicity, history of smoking, and age at last assessment. SLE: systemic lupus erythematosus; RP: Raynaud's phenomenon; SLICC/ACR: Systemic Lupus International Collaborating Clinics/American College of Rheumatology; GFR: glomerular filtration rate.

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