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Association of Discoid Lupus with Clinical Manifestations and Damage Accrual in PROFILE: A Multiethnic Lupus Cohort

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Abstract

Objective—To determine the clinical manifestations and disease damage associated with discoid rash in a large multiethnic systemic lupus erythematosus (SLE) cohort.

Methods—SLE patients (per ACR criteria), age ≥ 16 years, disease duration ≤ 10 years at enrollment, and defined ethnicity (African American, Hispanic or Caucasian), from a longitudinal cohort were studied. Socioeconomic-demographic features, clinical manifestations and disease damage [as per the Systemic Lupus International Collaborating Clinics Damage Index (SDI)] were determined. The association of DLE with clinical manifestations and disease damage was examined using multivariable logistic regression.

Results—A total of 2,228 SLE patients were studied. The mean (standard deviation, SD) age at diagnosis was 34.3 (12.8) years and the mean (SD) disease duration was 7.9 (6.0) years; 91.8% were women. Discoid lupus was observed in 393 (17.6%) of patients with SLE. In the multivariable analysis, patients with discoid lupus were more likely to be smokers and of African-American ethnicity, and to have malar rash, photosensitivity, oral ulcers, leukopenia and vasculitis. DLE patients were less likely to be of Hispanic (from Texas) ethnicity, and to have arthritis, end-stage renal disease (ESRD), and antinuclear, anti-dsDNA and anti-phospholipid antibodies. Patients with DLE had more damage accrual, particularly chronic seizures, scarring alopecia, scarring of the skin, and skin ulcers.

Conclusion—In this cohort of SLE patients, discoid lupus was associated with several clinical features including serious manifestations such as vasculitis and chronic seizures.

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Keywords

discoid rash; systemic lupus erythematosus; disease damage

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that presents with a wide spectrum of clinical manifestations ranging from skin rashes to severe and life-threatening complications. Skin involvement occurs in 70–85% of SLE patients and is classified according to morphology and histopathologic characteristics as specific and non-specific cutaneous lupus erythematosus (CLE) (1). Specific lesions include chronic CLE, subacute CLE and acute CLE. Discoid lupus (DLE) is the most common form of chronic CLE and may be the initial presentation of SLE in up to 10% of cases (2).

Skin lesions of DLE are mainly localized in sun-exposed areas and may lead to scarring and disfigurement. These patients rarely present with significant organ involvement and generally have a good prognosis (3,4). Nevertheless, the evolution to systemic lupus has been reported in 5–10% of cases (3,5). Previous works have focused on studying patients with isolated DLE; however, data evaluating the characteristics of SLE patients with DLE are limited. Therefore, we sought to determine the association of DLE with clinical manifestations and disease damage in a large multi-ethnic cohort of SLE patients.

Patients and Methods

As previously described, the Genetic Profile Predicting the Phenotype (PROFILE) is a well-characterized multi-ethnic prospective cohort of SLE patients constituted from multiple sites including the University of Alabama at Birmingham, John Hopkins University, Northwestern University, the University of Texas Health Science Center at Houston, and the University of Puerto Rico Medical Sciences Campus (6). The Institutional Review Board of each institution approved this study and written informed consent was obtained from all participating subjects according to the Declaration of Helsinki.

PROFILE patients meet the American College of Rheumatology (ACR) revised and updated criteria (7,8), are 16 years of age or older, and have disease duration ≤10 years at the time of enrollment. They are of defined ethnicity [Hispanic of Mexican ancestry (residing and enrolled in Texas, hence Texan Hispanics), Hispanic of Puerto Rican ancestry (residing and enrolled in Puerto Rico, hence Puerto Rican Hispanics), African-American, and Caucasian], having reported all four grandparents to be of the same ethnic background. There a total of 2,228 SLE patients followed longitudinally in PROFILE.

Variables

The PROFILE database consists of variables common to the individual cohorts identified after carefully mapping the different cohorts' databases (6). As previously described, this database includes variables from the socioeconomic-demographic, clinical, immunological and genetic domains. Only the variables included in this study will be described. Discoid lupus was ascertained according to the ACR classification criteria, based on morphologic characteristics (erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions) as documented by qualified and experienced rheumatologists during physical examination (7).

Socioeconomic-demographic variables evaluated included age at SLE diagnosis, age at last study visit, gender, ethnicity, years of education, health insurance, and smoking status. Time

of SLE diagnosis was defined as the date at which a patient met at least four ACR criteria. Disease duration was defined as the time between SLE diagnosis and last study visit.

The clinical variables included cumulative SLE-related clinical manifestations, autoantibodies, medications, comorbidities, and disease damage assessed with the Systemic Lupus International Collaborating Clinics Damage Index (SDI) (9). Clinical manifestations were examined as per the ACR classification criteria, as well as other selected clinical manifestations such as vasculitis and Raynaud's phenomenon. Antinuclear, anti-dsDNA, anti-Smith, and anti-phospholipid antibodies were locally measured. Cumulative exposure to glucocorticoids, hydroxychloroquine, cyclophosphamide, methotrexate, mycophenolate mofetil, and azathioprine was also examined. Selected comorbidities were recorded including hypertension (recording of three abnormal readings and/or the use of antihypertensive medications), coronary artery disease, cerebrovascular events, peripheral artery disease, venous thromboembolism, pulmonary hypertension, and hypothyroidism. The SDI score as well as the individual components of the SDI were also assessed.

Statistical analyses

Using a cross-sectional case-only approach, descriptive analyses were performed to compare the socioeconomic-demographic features, clinical variables and disease damage in SLE patients with and without discoid lupus. The relationship between variables was examined by Student's t tests or chi-square tests, as appropriate. The association of DLE with clinical manifestations and disease damage was examined using multivariable logistic regression adjusted for pertinent socioeconomic-demographic variables. Final multivariable models included independently selected variables with a p value ≤ 0.10 and pertinent socioeconomic-demographic variables and fit using maximum likelihood ratio methods. Variables with a $p \leq 0.05$ in these analyses were considered to be significant. All analyses were performed using SAS software, version 9.1 (SAS Institute, Cary, North Carolina, United States).

Results

At the time of analysis, 2,228 patients were included in the PROFILE cohort. The mean (standard deviation, SD) age at diagnosis was 34.3 (12.8) years and the mean (SD) disease duration was 7.9 (6.0) years; 91.8 % were females. The distribution of ethnic populations was as follows, 43.3% were Caucasians, 35.7% were African Americans, 9.9% were Puerto Rican Hispanics, 9.3% were Texan Hispanics, and other ethnic groups represented 1.8% of the cohort. Discoid lupus was observed in 393 (17.6%) of SLE patients. Of those with discoid rash, 75.8% were diagnosed prior to or at the time of SLE diagnosis. Of those with discoid rash diagnosed after SLE diagnosis, the mean (SD) time to diagnosis was 3.8 (5.1) years.

Table 1 shows the socioecononomic-demographic features in SLE patients with and without discoid lupus. SLE patients with DLE were predominantly women (92.1%) with a mean age at diagnosis [mean (standard deviation, SD)] of 34.5 (12.4) years. DLE was more common in African Americans (28.6%), followed by Caucasians (12.6%), Puerto Rican Hispanics (10.9%), and Texan Hispanics (6.2%) ($p < 0.001$). DLE patients were more likely to have longer disease duration (9.4 vs. 7.6 years, $p < 0.001$), fewer years of formal education (13.2 vs. 13.8 years, $p < 0.001$), and to have a positive history of smoking (23.2% vs. 13.7%, $p < 0.001$) compared to SLE patients without DLE. No significant differences were observed for age, gender and health insurance.

In Table 2 we show the association of DLE with clinical manifestations, immunologic features, selected comorbidities, and damage accrual in SLE patients after adjusting for

ethnicity, gender, disease duration, education, and smoking. Discoid lupus was associated with malar rash (odds ratio [OR] 1.28, 95% confidence interval [95% CI] 1.02–1.62), photosensitivity (OR 1.66, 95% CI 1.30–2.13), oral ulcers (OR 1.35, 95% CI 1.07–1.70), leukopenia (OR 1.46, 95% CI 1.16–1.83), and vasculitis (OR 1.62, 95% CI 1.22–2.13). Immunologic abnormalities such as positive ANA (OR 0.52, 95% CI 0.31–0.88), anti-phospholipid antibodies (OR 0.71, 95% CI 0.52–0.98) and elevated anti-dsDNA (OR 0.64, 95% CI 0.51–0.80) antibodies were less common among patients with DLE. Furthermore, arthritis was also less frequent in SLE patients with discoid lupus (OR 0.73, 95% CI 0.54–0.99). In addition, DLE patients were more likely to have a higher overall SDI score (OR 1.07, 95% CI 1.02–1.13) indicative of greater cumulative damage. There were no significant differences in the pharmacologic profile among SLE patients with and without discoid lupus after adjusting for ethnicity, gender, disease duration, education, and smoking (data not shown).

Because the SDI score was associated with DLE, we determined the relationship with the individual components of the SDI, again adjusting for ethnicity, gender, disease duration, education, and smoking (Table 3). Chronic seizures (OR 1.84, 95% CI 1.08–3.13), scarring alopecia (OR 5.71, 95% CI 3.91–8.35), extensive scarring of the skin (OR 14.66, 95% CI 8.67–24.81), skin ulcers (OR 2.43, 95% CI 1.06–5.60), and diabetes mellitus (OR 1.68, 95% CI 1.10–2.56) were associated with discoid lupus. However, SLE patients with discoid lupus were less likely to present end-stage renal disease (ESRD) (OR 0.42, 95% CI 0.19–0.93).

In Table 4 we present the results of the multivariable analysis including significant variables in the previous analysis plus ethnicity, gender, disease duration, and smoking. Model 1 includes SLE manifestations and the overall SDI. The following variables retained significance: Hispanic (Texas) ethnicity (OR 0.48, 95% CI 0.25–0.89), African American ethnicity (OR 3.57, 95% CI 2.70–4.71), disease duration (OR 1.04, 95% CI 1.02–1.06), education (OR 0.95, 95% CI 0.91–0.99), smoking (OR 1.89, 95% CI 1.41–2.54), photosensitivity (OR 1.85, 95% CI 1.40–2.46), arthritis (OR 0.65, 95% CI 0.48–0.89), leukopenia (OR 1.46, 95% CI 1.15–1.85), anti-dsDNA (OR 0.71, 95% CI 0.56–0.91), anti-phospholipid antibodies (OR 0.70, 95% CI 0.50–0.98), vasculitis (OR 1.53, 95% CI 1.13–2.05), and SDI score (OR 1.08, 95% CI 1.02–1.14. In model 2, which included SLE manifestations plus the individual components of the SDI (but not the overall SDI), Hispanic (Texas) ethnicity (OR 0.41, 95% CI 0.20–0.81), African American ethnicity (OR 3.18, 95% CI 2.38–4.24), disease duration (OR 1.05, 95% CI 1.03–1.07), smoking (OR 1.65, 95% CI 1.20–2.27), photosensitivity (OR 1.59, 95% CI 1.18–2.13), arthritis (OR 0.67, 95% CI 0.48–0.94), leukopenia (OR 1.41, 95% CI 1.09–1.81), anti-dsDNA antibodies (OR 0.66, 95% CI 0.51–0.85), chronic seizures (OR 1.92, 95% CI 1.03–3.60), ESRD (OR 0.30, 95% CI 0.13–0.74), scarring alopecia (OR 3.42, 95% CI 2.17–5.37), and extensive scarring of the skin (OR 10.76, 95% CI 5.89–19.66) remained significant.

Discussion

SLE patients presenting with discoid lupus have generally been regarded as having a mild form of disease mainly characterized by mucocutaneous involvement. Some studies have suggested that life-threatening manifestations are uncommon among these patients and that usually they have a better prognosis compared to SLE patients without DLE (4,10). Data are extensive in patients with isolated DLE; however, studies assessing the clinical characteristics of SLE patients with discoid lupus are limited. In the present study, we found that SLE patients with DLE were more likely to have malar rash, photosensitivity, oral ulcers, leukopenia, vasculitis, and more damage accrual including individual components of the SDI such as chronic seizures, scarring alopecia, extensive scarring of the skin, and skin ulcerations. Conversely, arthritis, ESRD, and immunologic abnormalities such as

antinuclear, anti-dsDNA, and anti-phospholipid antibodies were less common in patients with DLE.

Lupus is a heterogeneous disease characterized by a wide spectrum of clinical manifestations including discoid rash, which may occur with or without systemic involvement. There is evidence that genetic and environmental factors are involved in the pathogenesis of this complex disease (11–16). Genetic associations have been reported in patients with CLE including polymorphisms of genes encoding HLA, TNF-α, and complement molecules (12–15). Also, ethnicity has been shown to contribute to the heterogeneity of the clinical manifestations observed in SLE. For instance, the prevalence of DLE has been noted to vary among different ethnic populations (17,18). The overall frequency of discoid lupus in our cohort of SLE patients was nearly 18%. This prevalence is comparable with data from previous large cohort studies of DLE in SLE patients reporting an overall prevalence of around 14% in Latin American, African American, and white American populations (18). Conversely, Al-Attia reported a prevalence of discoid rash of 3% in a population of Arab patients with SLE (11), whereas Kapadia et al found it to be present in 57.5% of SLE patients from Pakistan (19), highlighting the broad range of frequencies of DLE among different ethnic groups. Furthermore, in our multiethnic cohort, African Americans more commonly had DLE as previously reported by other authors (20). Interestingly, our population of Hispanics from Texas was less likely to have discoid lupus when compared to other ethnic groups including Hispanics from Puerto Rico and Caucasians. This is a novel finding that contrasts a previous study assessing the clinical manifestations of SLE in Hispanic populations which shows similar rates of DLE among mestizos and Caucasians (21). However, SLE patients in this previous study included patients from different Latin American countries including Mexico, Guatemala and Peru, whereas our study included Hispanics mainly of Mexican ancestry. Taken together, these findings support the evidence that genetic factors contribute to the variability in the clinical expression of SLE.

In addition, the association of discoid lupus with cigarette smoking which has been widely recognized, was supported by our data (22). This finding underscores the important role of this environmental trigger in the pathogenesis of DLE, as an independently associated factor particularly among genetically predisposed individuals (22–25). Smoking has been previously linked to a shorter time-to-integument damage occurrence (26) and a significantly reduced clinical response in patients using antimalarials (27). It has been suggested that smoking may interfere with the accumulation of antimalarials within lysosomes, as well as with their metabolism thru enhancement of their elimination via the cytochrome P450 enzyme complex (28). However, in contrast to this observation recent studies have not shown a direct effect of cigarette smoking on response to antimalarials and suggest that other factors have a greater impact. Wahie S et al studied DLE patients treated with hydroxychloroquine and found that cigarette smoking did not have any significant influence on the response to this medication (29). Instead, they found that disseminated skin involvement and concomitant systemic disease were significantly associated with the lack of response to hydroxychloroquine. In addition, Leroux and colleagues found that cigarette smoking did not affect plasma levels of hydroxychloroquine in a population of SLE patients (30).

We, like other investigators, have found a high frequency of mucocutaneous involvement in patients with discoid lupus. Ng et al studied patients from a dermatological center in Singapore and found that the majority of SLE patients with DLE had oral ulcers, malar rash and photosensitivity, while only 20% had serious organ involvement (renal or central nervous system) (31). However, previous studies have shown an association of oral ulcers and photosensitivity with higher disease activity in patients with DLE, suggesting that these

manifestations must not be overlooked as they may herald a worse prognosis in patients with limited cutaneous involvement (32). Our cohort of SLE patients with discoid lupus presented more damage accrual compared to those without discoid lupus as measured by the SDI. The assessment of the individual components of the SDI revealed that the higher scores were mainly attributed to the skin damage caused by DLE.

We found a lower frequency of arthritis among patients with discoid lupus. These findings concur with previous studies that report a lower occurrence of arthralgias and arthritis in patients with chronic CLE (1,33). Of note, Tebbe et al showed that the presence of arthralgias was significantly associated to systemic disease among patients with cutaneous lupus (34). However, the latter study included patients from Germany and Austria, for which ethnic disparities must be taken into account when evaluating these findings. Furthermore, these patients were evaluated for the presence of arthralgias, whereas in our study an assessment was made for arthritis.

We found that SLE patients with DLE had a lower frequency of antinuclear, anti-dsDNA and anti-phospholipid antibodies compared to patients without discoid rash. This observation has been reported by other authors who have suggested that DLE appears to be associated with a lower frequency of immunologic markers of disease activity (4). However, the prevalence of anti-dsDNA antibodies in our patients with discoid rash (49.6%) was higher than that found in previous large cohorts of SLE patients with chronic CLE (30%) (1). Anti-dsDNA antibodies are usually regarded as a marker of systemic involvement (1) and have been related to widespread cutaneous disease and a higher prevalence of nephropathy and hemolytic anemia (34). Isotypes of anti-dsDNA antibodies have been associated to variable clinical expression in SLE; for example, Forger et al reported significant associations of the IgG isotype with lupus nephritis and the IgM isotype with cutaneous manifestations (36). Our data showed that discoid lupus was associated with less ESRD, and to a higher frequency of mucocutaneous manifestations and vasculitis. However, the isotypes of anti-dsDNA antibodies were not assessed in our cohort of lupus patients. Although our cohort of patients with DLE had a lower prevalence of anti-phospholipid antibodies, there were no significant differences in the prevalence of thromboembolic events when compared to SLE patients without discoid rash. Our data also revealed an association of discoid lupus with leukopenia, which contrasts with previous reports of lower frequencies of leukopenia in SLE patients with chronic CLE (1). This laboratory parameter is particularly important for patients with limited discoid rash because it has been identified as a marker of progression towards widespread disease and systemic involvement (5).

Vasculitis was more commonly seen among our patients with DLE. It has been reported that approximately 10–20% of lupus patients present with some form of vasculitis (37). However, our data contrast with previous studies reporting a lower frequency of this manifestation in SLE patients with chronic CLE (1). Of interest, Zecevic et al found that SLE patients with nonspecific cutaneous manifestations had significantly increased disease activity compared to those with only LE-specific lesions (38). Cutaneous vasculitis represents one of the LE-nonspecific skin manifestations and it has been shown to be the most frequent type of vasculitis in patients with SLE; also, it has been associated with activity of lupus and a worse prognosis (39–41). Callen et al reported a link between cutaneous vasculitis and the progression of disease as manifested by renal and central nervous system involvement (41). The association of discoid lupus with visceral vasculitis has been previously described in case reports. Nguyen et al reported a case of severe mesenteric and coronary vasculitis in a patient with chronic discoid lupus without other evidence of systemic involvement (42).

In agreement with other studies, we found that severe renal involvement, particularly ESRD, was less frequent in patients with discoid lupus (1,4). A plausible explanation for this finding is that our SLE patients with discoid lupus had a lower frequency of anti-dsDNA antibodies as compared to those without discoid rash. Anti-dsDNA antibodies bind glomerular collagen with high affinity and have been implicated in the pathogenesis of lupus nephritis (43); however, the exact mechanism remains controversial. Recent data suggest that immune complexes of chromatin fragments with anti-dsDNA antibodies and their subsequent binding to the glomerular basement membrane may represent a key event in the development of nephritis (44). However, no association was found between discoid rash and overall renal involvement among our cohort of patients with SLE. On the other hand, although less frequently, DLE patients with isolated disease may also present with renal involvement as shown in previous studies, mainly when having hypocomplementemia and disseminated cutaneous lesions, for which periodic monitoring is highly recommended for these patients (31,45).

Even though more skin damage was noted in our DLE patients thus accounting for higher SDI scores, these patients also presented other features leading to more damage accrual such as a higher frequency of chronic seizures. Neurological manifestations have been described in patients with discoid lupus. Koskenmies et al reported neurological involvement in 7.3% of patients with DLE as compared to 3.6% in SCLE; the majority of patients presenting epilepsy (33). Feinglass et al described an association of vasculitis with neuropsychiatric involvement (46). This observation was further supported by Karassa et al who reported a significant correlation of cutaneous vasculitic lesions with central nervous system involvement in SLE (47). Vasculitis of the brain vessels has been described in 7–15% of patients with neuropsychiatric lupus at autopsy; however, Johnson et al reported that neuropathological findings in these patients consist predominantly of changes related to small blood vessels, characterized by a non-inflammatory proliferative vasculopathy (48). In the study by Karassa et al, a negative correlation between neuropsychiatric manifestations and discoid lesions was established which contrasts with data from our study (47). Nonetheless, our findings together with other studies highlight the importance of cutaneous vasculitis as a possible marker of a worse prognosis in patients with discoid rash, placing them, perhaps, at increased risk for developing neurological complications such as seizures.

Some limitations of the present study should be addressed. First, an assessment of disease activity in this multiethnic cohort of SLE patients was not possible since the instruments used to measure this parameter were not homogenous throughout the study centers and even though the instruments used at the different centers are reliable, their scores cannot be converted. In addition, these data were not available for all study patients. Second, the assessment of the medication profile in our cohort is limited since information on the starting date of therapy of the individual medications and treatment duration were not available for all patients. This information is relevant for data analysis since early treatment certainly impacts the progression of disease. For example, antimalarials have been associated with decrease in disease flares (49) and integument injury (26), less damage accrual (50,51) and improved survival (52)among lupus patients. Third, antibodies were done locally when clinically indicated and not per protocol. Finally, we were not able to document the extension of skin involvement among patients with discoid lupus. The pattern of cutaneous involvement in DLE is particularly meaningful in terms of prognostic value. Widespread DLE has been associated with a higher frequency of laboratory abnormalities such as anemia, elevated erythrocyte sedimentation rate, high ANA titers and anti-dsDNA antibodies. In addition, widespread disease has been related to a higher prevalence of photosensitivity, panniculitis and systemic involvement (1,31).

In summary, we found that discoid lupus was associated with higher frequency of mucocutaneous manifestations (other than DLE), integument damage, leukopenia, vasculitis, and chronic seizures and lower frequency of arthritis, ESRD and immunologic abnormalities. We also corroborated the association of discoid lupus with smoking and African American ethnicity while describing, to our knowledge, for the first time a decreased risk of discoid lupus among Hispanics (from Texas). This is the largest study examining the clinical associations of discoid rash in patients with SLE. Our findings highlight the importance of surveillance of this population of SLE patients, particularly because of the association with serious manifestations such as vasculitis and chronic seizures.

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Significance & Innovations

- Studies assessing the clinical features of systemic lupus erythematosus (SLE) patients with discoid lupus are limited.
- This is the largest study examining the clinical associations of discoid rash in patients with SLE. These patients were more likely to have malar rash, photosensitivity, oral ulcers, integument damage, leukopenia, vasculitis, and chronic seizures, while having a lower frequency of arthritis, end-stage renal disease, and immunologic abnormalities.

Table 1

Socioeconomic-demographic features as a function of the presence of discoid lupus.

Feature	SLE with discoid lupus n=393	SLE without discoid lupus n=1835	p value
Ethnicity, %			
African American (n=793)	227 (28.6)	566 (71.4)	<0.001
Caucasian (n=966)	122 (12.6)	844 (87.4)	
Hispanic			
Puerto Rico (n=220)	24 (10.9)	196 (89.1)	
Texas (n=209)	13 (6.2)	196 (93.8)	
Other (n=40)	7 (17.5)	33 (82.5)	
Age at diagnosis, mean (SD) years	34.5 (12.4)	34.3 (12.9)	0.829
Disease duration, mean (SD) years	9.4 (6.9)	7.6 (5.8)	<0.001
Gender, n (%) female	362 (92.1)	1682 (91.7)	0.793
Years of education, mean (SD) years	13.2 (3.0)	13.8 (3.0)	<0.001
Health insurance (n=1580), n (%) having it	235/257 (91.4)	1189/1323 (89.9)	0.459
Currently smoking, n (%)	91 (23.2)	251 (13.7)	<0.001

SLE: systemic lupus erythematosus; SD: standard deviation

Table 2

Multivariable analyses of the association of discoid lupus with cumulative SLE manifestations, immunologic features, selective comorbidities, and damage accrual.

Feature	OR (95% CI)*	p value
ACR Criteria		
Malar rash	1.28 (1.02–1.62)	0.037
Photosensitivity	1.66 (1.30–2.13)	<0.001
Oral ulcers	1.35 (1.07–1.70)	0.011
Arthritis	0.73 (0.54–0.99)	0.040
Serositis	0.95 (0.76–1.19)	0.665
Renal involvement	0.80 (0.62–1.02)	0.067
CNS involvement	1.23 (0.88–1.72)	0.226
Seizures	1.26 (0.85–1.86)	0.249
Psychosis	1.31 (0.79–2.18)	0.299
Hematologic involvement		
Hemolytic anemia	0.95 (0.65–1.39)	0.786
Leukopenia	1.46 (1.16–1.83)	<0.001
Lymphopenia	0.85 (0.67–1.06)	0.154
Thrombocytopenia	0.91 (0.68–1.21)	0.528
Immunologic features		
Anti-nuclear antibodies	0.52 (0.31–0.88)	0.016
Anti-dsDNA antibodies	0.64 (0.51–0.80)	<0.001
Anti-Smith antibodies	1.15 (0.89–1.49)	0.287
Anti-phospholipid antibodies	0.71 (0.52–0.98)	0.040
Other SLE manifestations		
Vasculitis	1.62 (1.22–2.13)	<0.001
Raynaud's phenomenon	1.00 (0.80–1.25)	0.989
Transverse myelitis	-	-
Comorbidities		
Hypertension	1.02 (0.81–1.28)	0.879
Coronary artery disease	1.34 (0.77–2.32)	0.304
Stroke	1.21 (0.72–2.02)	0.477
Peripheral artery disease	1.12 (0.66–1.90)	0.679
Venous thrombosis	0.83 (0.55–1.26)	0.382
Pulmonary hypertension	0.97 (0.52–1.81)	0.924
Hypothyroidism	0.79 (0.53–1.19)	0.257
SDI	1.07 (1.02–1.13)	0.007

SLE: systemic lupus erythematosus; ACR: American College of Rheumatology; CNS: central nervous system; SDI: Systemic Lupus International Collaborating Clinics Damage Index;

*Adjusted odds ratio (OR) for ethnicity, gender, disease duration, education, and smoking; 95% CI: 95% confidence interval

Table 3

Multivariable analyses of the association of discoid lupus with the individual components of the Systemic Lupus International Collaborating Clinics Damage Index (SDI).

Feature	OR (95% CI)	p value
Ocular		
Cataracts	1.19 (0.83–1.70)	0.345
Retinal changes or optic atrophy	0.93 (0.51–1.72)	0.820
Neuropsychiatric		
Cognitive impairment	1.03 (0.71–1.48)	0.891
Chronic seizures	1.84 (1.08–3.13)	**0.025**
Cerebral vascular accidents	1.21 (0.76–1.92)	0.423
Cranial or peripheral neuropathy	0.53 (0.28–1.00)	0.051
Transverse myelitis	-	-
Renal		
GFR < 50%	0.86 (0.49–1.51)	0.590
Proteinuria 24hours, ≥ 3.5 grams	1.00 (0.66–1.51)	0.993
End-stage renal disease	0.42 (0.19–0.93)	**0.033**
Pulmonary		
Pulmonary hypertension	1.04 (0.55–1.96)	0.895
Pulmonary fibrosis	1.00 (0.56–1.78)	0.997
Shrinking lung	0.40 (0.05–3.14)	0.381
Pleural fibrosis	1.18 (0.52–2.69)	0.691
Pulmonary infarction	-	-
Cardiovascular		
Angina or coronary artery bypass	1.48 (0.73–2.99)	0.274
Myocardial infarction	1.82 (0.95–3.47)	0.071
Cardiomyopathy	1.62 (0.90–2.91)	0.110
Valvular disease or replacement	0.44 (0.17–1.14)	0.090
Pericarditis or pericardiectomy	0.74 (0.25–2.17)	0.577
Peripheral Vascular		
Claudication	0.73 (0.15–3.59)	0.696
Minor tissue loss	1.40 (0.59–3.33)	0.450
Significant tissue loss	0.88 (0.25–3.09)	0.841
Venous Thrombosis	0.45 (0.17–1.19)	0.109
Gastrointestinal		
Infarction or resection of bowel	1.16 (0.73–1.83)	0.527
Mesenteric insufficiency	0.79 (0.08–7.83)	0.840
Chronic peritonitis	1.93 (0.34–11.02)	0.460
Stricture or upper GI tract surgery	0.36 (0.05–2.84)	0.330

Feature	OR (95% CI)	p value
Pancreatitis	1.03 (0.21–5.01)	0.966
Musculoskeletal		
Atrophy or weakness	0.91 (0.43–1.94)	0.805
Deforming or erosive arthritis	1.06 (0.59–1.88)	0.848
Osteoporosis with fracture	1.19 (0.75–1.89)	0.454
Avascular necrosis	0.95 (059–1.52)	0.829
Osteomyelitis	0.57 (0.19–1.72)	0.315
Ruptured tendons	0.39 (0.11–1.39)	0.147
Skin		
Scarring **alopecia**	5.71 (3.91–8.35)	**<0.001**
Extensive scarring of the skin	14.66 (8.67–24.81)	**<0.001**
Skin ulcers	2.43 (1.06–5.60)	**0.037**
Premature gonadal failure	1.03 (0.64–1.66)	0.908
Diabetes mellitus	1.68 (1.10–2.56)	**0.016**
Malignancy	0.95 (0.52–1.72)	0.861

GFR: glomerular filtration rate, GI: gastrointestinal;

*Adjusted odds ratio (OR) for ethnicity, gender, disease duration, education, and smoking; 95% CI: 95% confidence interval

Table 4

Variables independently associated with discoid lupus by multivariable analyses

Feature	Model 1		Model 2	
	OR (95% CI)	p value	OR (95% CI)	p value
Ethnicity				
African American	3.57 (2.70–-4.71)	<0.001	3.18 (2.38–4.24)	<0.001
Hispanic, Puerto Rico	1.04 (0.63–1.70)	0.408	0.87 (0.52–1.46)	0.203
Hispanic, Texas	0.48 (0.25–0.89)	<0.001	0.41 (0.20–0.81)	<0.001
Other	1.65 (0.68–3.99)	0.425	1.85 (0.77–4.46)	0.193
Caucasian	Reference group		Reference group	
Disease duration	1.04 (1.02–1.06)	<0.001	1.05 (1.03–1.07)	<0.001
Education	0.95 (0.91–0.99)	0.018	0.96 (0.92–1.01)	0.091
Smoking	1.89 (1.41–2.54)	<0.001	1.65 (1.20–2.27)	0.002
Malar rash	1.21 (0.93–1.56)	0.152	1.13 (0.86–1.48)	0.383
Photosensitivity	1.85 (1.40–2.46)	<0.001	1.59 (1.18–2.13)	0.002
Oral ulcers	1.15 (0.89–1.47)	0.282	1.13 (0.87–1.47)	0.355
Arthritis	0.65 (0.48–0.89)	0.008	0.67 (0.48–0.94)	0.019
Leukopenia	1.46 (1.15–1.85)	0.002	1.41 (1.09–1.81)	0.008
Anti-nuclear antibodies	0.59 (0.34–1.03)	0.066	0.59 (0.32–1.07)	0.083
Anti-dsDNA antibodies	0.71 (0.56–0.91)	0.006	0.66 (0.51–0.85)	0.001
Anti-phospholipid antibodies	0.70 (0.50–0.98)	0.040	0.73 (0.51–1.04)	0.077
Vasculitis	1.53 (1.13–2.05)	0.005	1.26 (0.91–1.74)	0.171
SDI	1.08 (1.02–1.14)	0.011	---	---
SDI components				
Chronic seizures	---	---	1.92 (1.03–3.60)	0.041
End-stage renal disease	---	---	0.30 (0.13–0.74)	0.009
Scarring alopecia	---	---	3.42 (2.17–5.37)	<0.001
Extensive scarring of skin	---	---	10.76 (5.89–19.66)	<0.001
Skin ulcers	---	---	0.90 (0.31–2.64)	0.853
Diabetes mellitus	---	---	1.27 (0.77–2.07)	0.346

Model 1 includes systemic lupus erythematosus (SLE) manifestations and the overall SDI.

Model 2 includes SLE manifestations and the individual components of the SDI. Gender was also included in both multivariable models. OR: odds ratio; 95% CI: 95% confidence interval; SDI: Systemic Lupus International Collaborating Clinics Damage Index.