The Effect of Race on Disease Activity in Systemic Lupus Erythematosus

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ABSTRACT. ***Objective.*** To determine and contrast the disease activity and clinical variables between Hispanic and Caucasian patients with systemic lupus erythematosus (SLE) in New Mexico.

Methods. Socioeconomic-demographic and clinical data were collected from 125 SLE patients by an interview-administered questionnaire. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) was used to assess disease activity.

Results. Seventy-four Hispanics (H) and 40 Caucasians (C) were compared. Demographics including age, gender, disease duration, marital status, and cigarette smoking were similar between the 2 groups. However, education and income were higher in the Caucasian group compared to the Hispanic group. There was no significant difference between the 2 groups in overall disease activity as measured by the SLEDAI. However, when individual components of the SLEDAI were compared, Hispanics had an increased prevalence of arthritis (77% vs 51%, p = 0.01) and depressed complement levels (40% vs 18%, p = 0.02). Moreover, corticosteroid use was higher among the Hispanics compared to the Caucasian population (p = 0.03).

Conclusion. We found similar levels of overall disease activity in Hispanic and Caucasian patients with SLE. However, Hispanics used more corticosteroids, had a greater prevalence of arthritis, and had depressed complement levels indicating increased SLE disease activity highly restricted to specific domains. It remains to be determined whether these restricted but discrete differences are genetic in origin, or are related cultural or environmental factors. (J Rheumatol 2004;31:915–9)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS ETHNICITY HISPANIC
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As frequently noted in the literature, systemic lupus erythematosus (SLE) tends to affect nonwhite populations more severely than whites, as manifested by increased disease activity, more frequent and more severe organ system involvement, and a lower probability of survival[1-15]. The cause of the disparity has not been clearly established, although differences in socioeconomic status, environment, biologic features, and genetics have been proposed[1-15].

Over the last 30 years the United States has seen a large increase in the number of residents who trace their origins back to Hispanic countries[1]. Data on the characteristics of SLE among US Hispanic Americans have come from many well-designed studies by the LUMINA (Lupus in Minority populations: Nature vs nurture) cohort[2-8]. Reveille, *et al*[2] found that Hispanics had a higher Systemic Lupus Activity Measure (SLAM) than Caucasians although the difference was not statistically significant. Hispanics were more likely to have had an abrupt onset of SLE onset compared to African-Americans and Caucasians. The study also showed that Hispanics were more likely to have cardiac and renal disease, as well as a higher physician's global assessment of disease activity. Alarcon, *et al*[3] found Hispanics and African-Americans had higher SLAM scores than Caucasians. In that study, Hispanics also had lower socioeconomic status than white participants. The SLAM scores remained significantly higher in the non-Caucasians even after adjusting for socioeconomic and behavioral/psychological features. The analysis of the data grouped African-Americans and Hispanics together compared with Caucasians.

In this study, we compared both overall disease activity and specific clinical components of activity between the New Mexico Hispanic and Caucasian populations.

MATERIALS AND METHODS

Study population and research design. The study cohort included 125 well-characterized SLE outpatients randomly selected from the University of New Mexico Systemic Lupus Data Base. Exclusion criteria included individuals less than 18 years old, SLE-overlap disease, individuals greater

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than 65 years old, and SLE of less than one year's duration. Of these 125 patients, 114 both qualified for the study and agreed to participate. The diagnosis of SLE was confirmed in each patient using the American Rheumatism Association 1982 and American College of Rheumatology 1997 revised criteria[16,17]. A rheumatologist confirmed the diagnosis of SLE after an in-depth face-to-face interview, medical history, physical examination, chart-review, and appropriate laboratory testing. A single interviewer collected all epidemiologic data using an individual interview and a standardized questionnaire form designed to record the following demographic details: ethnicity, cigarette smoking, alcohol consumption, education, income, and other clinical variables.

Determination of SLE activity. The SLE disease activity index (SLEDAI) was used to estimate SLE disease activity[18]. All SLEDAI scores were obtained by one rheumatologist after an in-depth interview, physical examination, and laboratory assessment. Since this study was concerned with longterm rather than point-in-time effects on disease activity, 3 scores from each index for each patient were obtained over a period of 6 months (at 0, 3, and 6 months) and averaged to obtain a mean SLEDAI score. These mean disease activity scores were then used for subsequent analyses. In addition, the use of prednisone and hydroxychloroquine therapy were obtained at each visit. The patient's dose of prednisone on the day the SLEDAI was done was recorded (at 0, 3, and 6 months) and averaged to obtain a mean prednisone dose. The mean erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were also obtained.

Characterization of epidemiologic data. The ethnicity was asked of all patients by a single interviewer (4 grandparents of the same ethnic background as defined in previous studies[2]. Detailed smoking data were collected allowing classification of patients into 3 smoking status groups: (1) never smoker; (2) ex-smoker (defined by no smoking for one year prior to the interview date); and (3) current smoker (as defined as in prior studies by smoking at least one cigarette a month for at least 3 consecutive months prior to the interview date). Alcohol consumption per week (one average drink was defined as 12 ounces of beer, one glass of wine, or 4 ounces of liquor) over the past year was also recorded. The number of years of school completed (not completing high school/completion of high school/college or college graduate) and approximate household income over the past year were also collected.

Statistical analysis. Data were entered into Excel (Version 97, Microsoft, Seattle, WA, USA), and analyzed in SAS (SAS/STAT Software, Release 6.11, Cary, NC, USA)[19]. The comparison between the 2 ethnic groups was done by Student's t test for continuous variables and by Fisher's exact test for categorical variables. The adjustment for potentially confounding variables, in the above analyses, was done by analysis of covariance. The adjustment for covariates when the outcome was binary was done by multivariate logistic regression.

RESULTS

Characteristics of the patients are shown in Table 1. The mean age ± standard deviation (SD) of the 2 groups was 42.3 ± 15.6 (Hispanics) and 46.6 ± 10.4 (non-Hispanic Caucasians). The mean duration ± SD of SLE was 7.58 ± 6.8 for Hispanics and 9.25 ± 8.3 for Caucasians. Ninety-seven (97%) were female. Hispanics had a lower level of education ($p = 0.001$) and a lower level of income level ($p = 0.02$) than Caucasians. There was no significant difference in age of onset of SLE, duration of SLE, and marital status. There was also no significant difference in smoking status, alcohol use, and hydroxychloroquine use between the 2 ethnic groups. Among Hispanics 44 (59%) people were taking prednisone compared to 15 (38%) Caucasians ($p = 0.03$). The mean prednisone dose ± SD was 7.6 ± 11.0 and 6.6 ± 13.0, respectively ($p = 0.70$). The mean SLEDAI scores among the 2 groups are shown in Table 2. The mean SLEDAI ± SD for Hispanics (11.16 ± 6.53) was not significantly different from Caucasians (11.20 ± 8.21) ($p = 0.98$). There was also no difference in SLEDAI between the 2 ethnic groups after adjusting for the frequency of prednisone, mean prednisone dose, and current smoking.

Individual components of the SLEDAI for the respective groups are shown in Table 2. As can be seen, a difference in frequency of individual SLEDAI components reaches statistical significance in only 2 domains: (1) arthritis and (2) depressed complement levels. Hispanics had a frequency of arthritis in 77% compared to 51% of non-Hispanic Caucasians ($p = 0.01$). Hispanics had a frequency of depressed complement levels in 40% compared to 18% of Caucasians ($p = 0.02$). This remained statistically significant even after controlling for age and duration of SLE ($p = 0.02$). The depressed complement levels were further subdivided into C3 and C4 individually. Hispanics had a lower overall mean C3 (100 ± 31.06) compared to non-Hispanic Caucasians (116 ± 33.58) ($p = 0.02$). Hispanics also had a lower overall mean C4 (20 ± 9.30) compared to non-Hispanic Caucasians (25 ± 11.68) ($p = 0.04$). As a group, 60% of those who had arthritis were taking prednisone versus 32% who did not have arthritis ($p = 0.008$). As a group, 69% of patients with depressed complement levels were taking prednisone versus 40% of those with normal complements ($p = 0.02$). There was no significant difference in mean ESR or CRP between the 2 groups.

DISCUSSION

In our study of 114 patients followed in a university rheumatology clinic, Hispanics and non-Hispanic Caucasians were very similar in overall SLE disease activity as measured by the SLEDAI. However, a significant difference was found between Hispanics and non-Hispanic Caucasians in certain measures of SLE disease activity, specifically an increased prevalence of arthritis and low complement in the former group. The increased use of prednisone by Hispanics, which is often used to treat the arthritis and myalgias of SLE, lends credence to the contention that these differences are real and actually have an impact on disease therapy. Supporting this interpretation, the group of patients who had arthritis and depressed complement levels used prednisone at a higher frequency.

There have been a number of studies that have examined different associations between ethnicity, SLE activity, and outcome[1-15]. In one study[4], SLAM scores were statistically significantly higher among African-Americans and Hispanics. With respect to the SLAM patient's global assessments, values in the Hispanics were closer to those in the Caucasians. Results of the final regression model of variables associated with higher SLAM scores did not include Hispanics but included African-American ethnicity,

Table 1. Demographics of study group (n = 114).

	Hispanic	Caucasian	p
N	74	40	
Women	72	38	
Men	2	2	
Mean current age, yrs ± SD	42.3 ± 15.6	46.6 ± 10.4	0.08
Mean age at SLE diagnosis, yrs ± SD	34.7 ± 15.3	37.4 ± 11.1	0.29
Mean duration of SLE, yrs ± SD	7.60 ± 6.8	9.25 ± 8.3	0.28
Past education, %			0.001
Never completed high school	23	15	
Completed high school	47	30	
College or college graduate	30	55	
Past income (USD)*, %			0.02
< 25,000	72	40	
25–50,000	15	45	
> 50,000	11	13	
Marital status, %			0.51
Never married	22	13	
Married/living with someone	48	57	
Divorced/widowed/separated	30	30	
Smoking status, %			0.88
Never smoker	32	37	
Ex-smoker	34	33	
Current smoker	34	30	
Hydroxychloroquine use, %	32	33	1.00
Corticosteroid use, %	59	38	0.03
Mean corticosteroid dose, mg/day ± SD	7.6 ± 11.0	6.6 ± 13.0	0.70

* 3 patients refused to answer this question

Table 2. Frequency of individual SLEDAI items and total mean SLEDAI values.

Manifestation	Hispanic %	Caucasian %	p
Seizure	7.1	5.1	NS*
Psychosis	2.9	7.7	NS
Organic brain syndrome	14.3	23.1	NS
Visual disturbance	1.4	0	NS
Cranial nerve disorder	0	0	NSD#
Lupus headache	30	38	NS
CVA	0	0	NS
Vasculitis	7.1	5.1	NS
Arthritis	77.1	51.3	0.01
Myositis	0	0	NSD
Urinary casts	0	0	NSD
Hematuria	0	5.1	NS
Proteinuria	7.1	10.3	NS
Pyuria	0	0	NSD
New rash	38.6	30.8	NS
Alopecia	8.6	12.8	NS
Mucosal ulcers	42.9	48.7	NS
Pleurisy	37.1	48.7	NS
Pericarditis	0	2.6	NS
Low complement	40	17.9	0.02
Increased DNA	12.8	11.4	NS
Thrombocytopenia	11.4	7.7	NS
Leukopenia	12.9	28.2	NS
Fever	2.9	2.6	NS
Mean SLEDAI ± SD	11.16 ± 6.53	11.20 ± 8.21	NS

* Not significant, # insufficient data, SD: standard deviation.

lack of private health insurance, abrupt disease onset, presence of anti-Ro antibodies, higher levels of helplessness, and abnormal illness-related behaviors. Karlson, *et al* found no effect of race (comparing African-Americans and Caucasians) on outcome in SLE in a study designed to eliminate the confounding variable of socioeconomic status with race[14].

Hispanics had significantly depressed complement levels compared to Caucasians in our study. This finding remained significant even after analyzing C3 and C4 separately. To the best of our knowledge, this has not previously been reported. Molina, *et al* compared African-American with Colombian SLE patients, and found a higher frequency of anti-Sm, anti-RNP, and anti-Ro positivity among African-American patients compared with Colombians[10]. However, there was no significant difference in depressed complement levels between the 2 ethnic groups. Ballou found serum C3 levels were more often depressed in the younger age group in one study, regardless of race (Caucasians and African-Americans were compared)[12]. Even after controlling for age in our study, there was a significant difference in depressed complement levels in Hispanics. Whether the increased frequency of low complement levels observed among our Hispanic population can be generalized to other Hispanic SLE patients cannot be determined at this time. In one study of 132 Puerto Rican patients with SLE, low C3 and C4 were observed in 38.3% and 35.7% respectively[15], similar to our findings (40% in our Hispanic population).

Interestingly, we did not find a significant difference in overall disease activity between our Hispanic and Caucasian population. There was no significant difference in overall SLEDAI even after adjusting for the frequency of patients taking prednisone and the mean prednisone dose between the 2 groups. It is not entirely clear why we did not find even a trend toward higher disease activity in our Hispanic population. Both our ethnic groups live in the same approximate geographic location with access to the same healthcare. Also, despite the fact that Hispanics had a lower education and income level overall, there was surprisingly no significant difference in smoking status between the 2 groups. Current cigarette smoking has been found to be associated with a higher disease activity even after adjusting for ethnicity, income level, and education level[20]. In addition, in one study mentioned above, abnormal illness behaviors such as smoking, not Hispanic ethnicity, were found to be in the final model predictive of disease activity ($p = 0.009$)[4]. Also, a majority of our Hispanic population had a Spanish background rather than strictly a Mexican ancestry.

As with all cross-sectional investigations, our study has certain limitations and potentials for bias. However, obvious sources of bias associated with selection of patients were minimized by (1) prospectively rather than retrospectively acquiring the data, (2) randomly selecting the patients from a well-characterized SLE cohort, (3) not using self-reporting of the diagnosis of SLE, but rather by having the diagnosis of SLE confirmed by laboratory testing and careful examination of the patient by a rheumatologist, (4) SLEDAI scores being determined independently by independent observers (interviewer and rheumatologist, respectively), and (5) the true cross-sectional nature of the study with very few patients in the SLE cohort refusing to participate. Recruitment/response rates were excellent for this study, with 91% both qualifying for the study and agreeing to participate.

The SLEDAI is a validated tool used to assess disease activity with ethnicity and other demographic variables[21,22]. Bias was minimized by using a single experienced rheumatologist who prospectively calculated all SLEDAI scores after a detailed history, physical examination, and laboratory testing, and not by retrospective review of notes or charts. Disease activity in SLE over its entire duration is variable, and thus we did not obtain one single SLEDAI value at a single point in time, but rather 3 points over a 6-month period. Other factors are known to influence the outcome in SLE such as socioeconomic status and cigarette smoking[22-25]. We obtained a detailed smoking history, and thus were able to control for this as well as other socioeconomic variables. One variable that was not controlled in this study was acculturation. Although not statistically significant, Alarcon found that poorly acculturated patients interestingly tended to have lower disease activity[7].

Our study found similar levels of overall disease activity in Hispanics and Caucasians. However, even allowing for the potential sources of bias discussed above, our data suggest there is a significant difference between Hispanics and Caucasians in certain measures of SLE disease activity, specifically, an increased prevalence of arthritis and low complement in the former group. The fact that there is also an increased use of corticosteroids in Hispanics suggests that these differences in activity, although restricted to limited clinical domains, have important clinical and therapeutic consequences. It remains to be determined whether these restricted but discrete differences are genetic in origin, or are related cultural or environmental factors. Further studies regarding ethnicity and SLE are required.

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