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Lupus in Hispanics: A matter of serious concern

ABSTRACT

Systemic lupus erythematosus in US Hispanics is a serious disease with devastating consequences. Prompt diagnosis is of paramount importance to prevent early organ damage and death. The authors review the salient features of lupus in US Hispanics and its short-term and long-term impact in order to raise physician awareness.

KEY POINTS

Amerindian genes contribute to a greater susceptibility to lupus, although there is an interplay between genetic and nongenetic factors in its etiology and expression.

In large studies, disease activity and organ damage were greater in African Americans and in Hispanics from Texas than in Caucasians and Hispanics from Puerto Rico.

Hispanics of primarily Amerindian ancestry (which includes Aztec, Mayan, Quechuan, Aymaran, and other Central and South American groups) have a lower survival rate than patients in other ethnic groups, but poverty is the responsible factor.

The need to control disease activity with corticosteroids must be balanced against the risk of overtreatment and organ damage.

Antimalarial drugs such as chloroquine and hydroxychloroquine should be prescribed from the outset to all patients with lupus, according to current guidelines designed to avoid ocular toxicity.

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Some diseases are either more serious or more frequent in US Hispanics, and systemic lupus erythematosus is one of them. This fact has not yet diffused to all providers, many of whom will be the ones dealing with these individuals when the disease first emerges.

In order to raise physicians' awareness of this situation, we will briefly review here the salient features of lupus in US Hispanics and its short-term and long-term impact.

HISPANICS ARE THE LARGEST MINORITY IN THE UNITED STATES

Over the last 30 years, the Hispanic population in the United States has increased to the point that it is now the largest US minority group, and the fastest-growing. In the 2010 US census, Hispanics surpassed the 50 million mark.[1] Physicians and health care providers are becoming familiar with this growing population and its ailments, but more needs to be done to familiarize them with specific conditions that are more frequent and more serious in US Hispanics.

No population-based study has yet defined the prevalence and incidence of lupus in US Hispanics. However, on the basis of hospital and outpatient visits in regions in which Hispanics make up a large part of the population, it has been inferred that this group has a higher frequency of lupus, probably as high as in African Americans.

Likewise, clinicians taking care of these patients have suspected that lupus is more severe in US Hispanics than in non-Hispanic Caucasians, but this was documented and brought to general attention only with the publication of reports from the Lupus in Minorities: Nature versus Nurture (LUMINA) study.[2]

LUMINA, a longitudinal study

LUMINA is a longitudinal study of 640 patients with lupus from four populations: Hispanic from Texas, Hispanic from Puerto Rico, African American, and Caucasian non-Hispanic (TABLE 1). At the time of recruitment, patients were at least 16 years old and had had lupus for 5 years or less. They come in for periodic visits to the University of Alabama at Birmingham, the University of Texas Health Science Center at Houston, and the University of Puerto Rico Medical Sciences Campus. Recruitment began in 1994 and finished in 2007. Follow-up ranges from 1 to 14 years, with a mean of 4.5 years.

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The purpose of the study is to shed light on the interplay of genetics and environment in this disease and, in the process, to raise awareness about the problem of lupus in Hispanics. In fact, much of the information in the following sections is from the LUMINA study.

TABLE 1

Baseline features of patients with lupus in the LUMINA study

FEATURE	TEXAS HISPANIC	PUERTO RICO HISPANIC	AFRICAN AMERICAN	CAUCASIAN NON-HISPANIC
Number of patients	118	102	234	181
Women	93%	95%	89%	85%
Mean age, years	33	37	35	41
Mean years of education	11	15	13	14
Married	54%	59%	33%	73%
Below poverty line [a]	42%	30%	45%	15%
With health insurance	50%	99%	81%	87%
Mean disease duration, months	16	19	16	18
Acute onset	27%	4%	17%	9%
Mean no. of criteria met	6	5	6	5
Renal disorder	62%	26%	62%	25%
Mean SLAM-R score [b]	11	7	11	8
Mean SDI score [c]	0.6	0.3	1.0	0.7
Mean SDI score (last visit)	2.2	0.5	2.3	1.4

[a] Adjusted for the number of household members
[b] Systemic Lupus Activity Measure; possible scores range from 0 (best) to 81 (worst)
[c] Systemic Lupus International Collaborating Clinics Damage Index; possible scores range from 0 (best) to 45 (worst)

UNPUBLISHED INFORMATION FROM THE LUPUS IN MINORITIES: NATURE VS NURTURE STUDY.

HISPANICS ARE NOT A HOMOGENEOUS GROUP

In the United States, the term *Hispanic* describes anyone whose origin goes back to a Spanish-speaking country. However, US Hispanics are not a homogeneous racial group: they differ in genetics, culture, and problems.

The largest US Hispanic subgroup and the one more likely to be seen by US physicians is Hispanics of Mexican origin, who account for 66% of all US Hispanics. This group has a higher percentage of Amerindian genes than those of Puerto Rican ancestry.[3] LUMINA researchers analyzed the DNA of 492 patients and found the following mixtures of genes[3]:

- Hispanics in Texas (mostly of Mexican origin): 48% Amerindian, 18% African, 34% European
- Hispanics from Puerto Rico: 20% Amerindian, 45% African, 35% European
- African Americans: 0% Amerindian, 79% African, 21% European
- Non-Hispanic Caucasians: 10% Amerindian, 18% African, 72% European.

Latin Americans of mixed European and Amerindian ancestry (which includes Aztec, Mayan, Quechuan, Aymaran, and other Central and South American groups) are called *mestizos*. Not all people in Latin America are mestizos: some are of European, African, or Asian ancestry, but in the United States they are all called Hispanics.

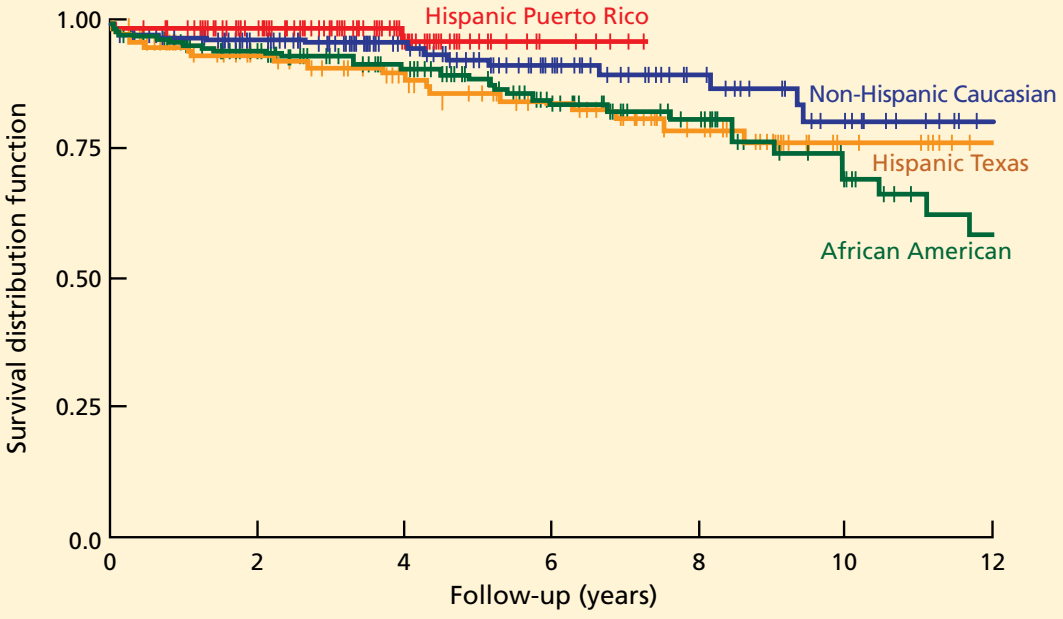

FIGURE 1. Kaplan-Meier survival curves for LUMINA patients as a function of ethnic group. African Americans and Texas Hispanics had a lower probability of survival than non-Hispanic Caucasians and and Puerto Rico Hispanics (log rank = 9.687; $P = .021$).

FERNÁNDEZ M, ALARCÓN GS, CALVO-ALÉN J, ET AL; LUMINA STUDY GROUP. A MULTIETHNIC, MULTICENTER COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AS A MODEL FOR THE STUDY OF ETHNIC DISPARITIES IN SLE. ARTHRITIS RHEUM 2007; 57:576–584.

Hispanics are the largest and fastest-growing minority group in the United States

LUPUS DIFFERS AMONG SUBGROUPS

LUMINA research has revealed that lupus is heterogeneous also among US Hispanic subgroups. When people from Puerto Rico get lupus, it is generally less serious and devastating than in those from Mexico or Central America. Since US Hispanics of Mexican or Central American origin possess more Amerindian genes, this observation supports the notion that these genes are important contributors to the occurrence and expression of the disease.

Amerindian genes contribute to a greater susceptibility to lupus,[4,5] although there is an interplay between genetic and nongenetic factors in the etiology and expression.[6] Lupus starts at a younger age in Hispanics of predominantly Amerindian ancestry than in non-Hispanic Caucasians, and the onset is more likely to be acute.[7]

Renal involvement in these patients[8] and mestizos from Latin America is rather common, probably as common as it is in US African Americans, and it tends to develop earlier than in non-Hispanic Caucasians.[9] Amerindian ancestral genes, like African genes, contribute to the occurrence of renal disease in lupus patients.[4] Furthermore, once nephritis ensues, end-stage renal disease occurs more often in US Hispanic and African American than in non-Hispanic Caucasian children, as demonstrated by Hiraki et al[10] using national databases, and the same is true in adults, as shown in the LUMINA cohort.[11]

Other potentially serious manifestations of the disease are also more common, including hematologic and central nervous system manifestations. Not surprisingly, then, these patients show a higher degree of disease activity, both early in the course of the disease[12,13] and over time.[14]

TABLE 1 compares the demographic and

clinical features of LUMINA patients according to ethnicity. By and large, Hispanics from Texas have lower levels of education and income (comparable with levels in African Americans), and this can adversely affect the disease course by limiting these patients' access to adequate care.[15]

DISEASE ACTIVITY AND ORGAN DAMAGE ARE GREATER IN HISPANICS

Disease activity in lupus reflects the ongoing immune-mediated inflammatory process. In LUMINA patients, regardless of the time at which disease activity was ascertained, it was higher in Hispanics from Texas and in African Americans than in non-Hispanic Caucasians and in Hispanics from Puerto Rico.[7,12,16–18] Similar findings were seen in the *Grupo Latinoamericano de Estudio de Lupus* (GLADEL) cohort,[13] in which mestizos and Hispanics of mixed African and European ancestry had higher maximum disease activity scores than non-Hispanic Caucasians.[13]

In addition, organ damage in lupus—the irreversible changes that occur in organ systems as a consequence of the disease or its treatments (eg, glucocorticoids, immunosuppressive drugs)—is more severe and develops sooner in Hispanics from Texas than in other groups.[6,18,19] Using multivariate analysis, LUMINA investigators[19] estimated the hazard ratio for the time until organ damage appeared for various risk factors, with values of 1 or greater indicating a shorter time and lower values indicating a longer time. Being a Hispanic from Texas carried a hazard ratio of 2.11 (95% confidence interval 1.15–3.88).

Because organ damage is an important and independent predictor of further damage[20] and death,[21] physicians need to take this disease quite seriously and try to prevent damage early in people at risk. To achieve that, the need to control disease activity must be balanced against the risk of overtreatment, as the important contribution of glucocorticoids to organ damage is well recognized.[22]

HISPANICS HAVE MORE COMORBIDITIES

Obesity, hypertension, diabetes, and metabolic syndrome are more common in US Hispanics, particularly those of Amerindian ancestry, than in the majority population of non-Hispanic Caucasians.[23,24] The potential deleterious effects of glucocorticoids in patients already predisposed to these conditions need to be considered, balancing adequate disease control against the potential adverse effects.[22]

TABLE 2

Poverty is the strongest predictor of death in patients with lupus[a]

VARIABLE	ODDS RATIO	95% CONFIDENCE INTERVAL	*P* VALUE
Age	1.024	1.003–1.046	.023
Male sex	1.279	0.572–2.858	
Ethnicity[b]			
Texan Hispanic	1.193	0.536–2.657	
Puerto Rican Hispanic	0.329	0.041–2.536	
African American	0.879	0.415–1.863	
Poverty[c]	2.109	1.236–3.517	.006
SLAM-R score at baseline visit[d]	1.144	1.103–1.186	< .001
SDI score at baseline visit[e]	1.186	1.016–1.386	.031

[a]Multivariate Cox proportional hazard regression analysis of mortality at 10 years in LUMINA (Lupus in Minorities, Nature versus Nurture) study patients
[b]Compared with non-Hispanic Caucasians as the reference group
[c]As defined by US federal government guidelines
[d]SLAM-R = Systemic Lupus Activity Measure revised
[e]SDI = Systemic Lupus International Collaborating Clinics Damage Index

FERNÁNDEZ M, ALARCÓN GS, CALVO-ALÉN J, ET AL; LUMINA STUDY GROUP. A MULTIETHNIC, MULTICENTER COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AS A MODEL FOR THE STUDY OF ETHNIC DISPARITIES IN SLE. ARTHRITIS RHEUM 2007; 57:576–584.

QUALITY OF LIFE IS WORSE WITH LUPUS

Whether it is measured with a generic instrument such as the Short Form 36 (SF-36), as it was in LUMINA,[25] or with a disease-specific tool such as the Lupus-Pro, quality of life is significantly worsened by lupus. Furthermore, Fernandez et al[26] found that a low level of health-related quality of life, as measured by the SF-6D version of the SF-36, was predictive of poor outcomes in LUMINA patients.

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An antimalarial drug increases survival in patients with lupus

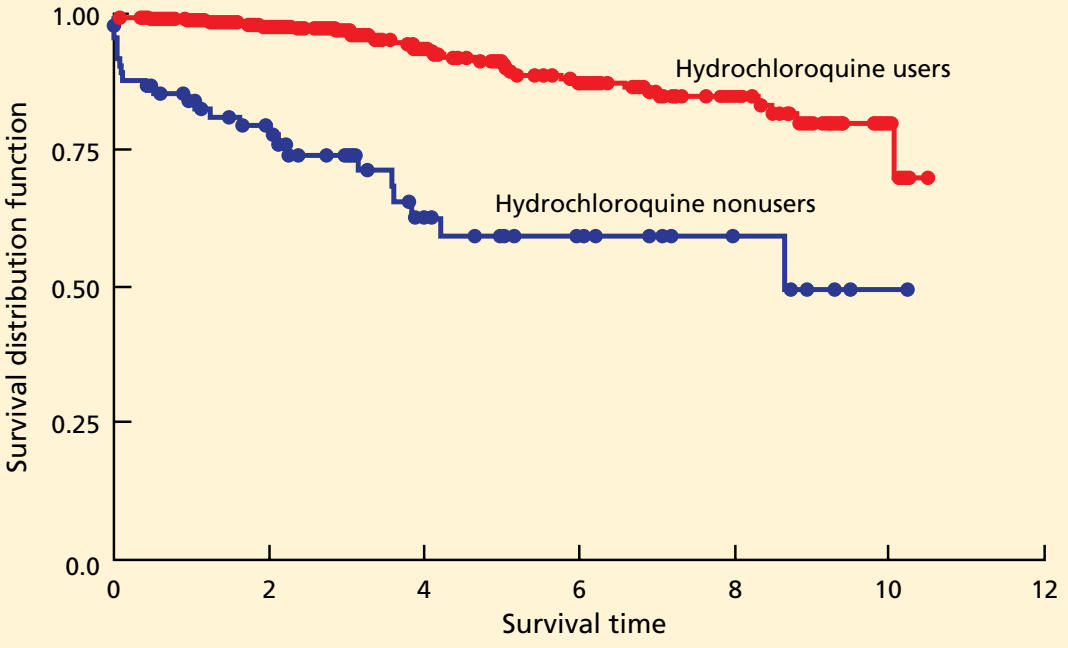

FIGURE 2. Kaplan-Meier survival curve as a function of hydroxychloroquine use.

DRAWN FROM DATA FROM ALARCÓN GS, MCGWIN G, BERTOLI AM, ET AL; LUMINA STUDY GROUP. EFFECT OF HYDROXYCHLOROQUINE ON THE SURVIVAL OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM LUMINA, A MULTIETHNIC US COHORT (LUMINA L). ANN RHEUM DIS 2007; 66:1168–1172.

LUMINA includes 640 patients with lupus from four US ethnic groups

POVERTY, NOT ETHNICITY, ACCOUNTS FOR HIGHER MORTALITY RATE

As yet, we have no population-based data comparing survival in US Hispanic patients with lupus vs that of other population groups.

At first inspection, data from LUMINA indicate that Hispanics of primarily Amerindian ancestry have a lower survival rate than patients in other ethnic groups (FIGURE 1).[6] However, when all other factors are taken into consideration, poverty, not ethnicity, is the major contributing factor (TABLE 2).[6,27]

This finding illustrates the important interplay between genetic and nongenetic factors in the course and final outcome of lupus, as already alluded to, although the exact relationship between them is not clear. It remains to be determined whether poverty is only a proxy for other population characteristics such as illiteracy, limited access to specialized care, limited access to medications, or cultural beliefs that may interfere with proper care.

ANTIMALARIAL DRUGS INCREASE SURVIVAL

Using statistical analysis that adjusts for confounding by indication, we and others[28–30] have shown that antimalarial drugs exert an independent and important protective effect on survival in lupus (FIGURE 2).

Important also is the protective effect of antimalarials on organ damage and the possibility of using them from disease outset in Hispanic patients at risk of early and rapid damage accrual,[11] renal damage, and even lupus nephritis.[31,32] This has very practical implications for the adequate and prompt management of these Hispanic patients.

PRACTICAL IMPLICATIONS

Lupus in US Hispanics is a serious disease with devastating consequences. Prompt diagnosis is paramount to prevent early organ damage and to prolong survival.

The disease may present in many different and unexpected ways, but joint pain, sun-sensitive rashes, renal involvement, cytopenias, and other manifestations should prompt the clinician to consider lupus in the differential diagnosis. Patients are often dismissed as having "arthritis" without being asked about other manifestations that may suggest a systemic connective tissue disease such as lupus. The same goes for skin rashes or unusual central nervous system manifestations.

The diagnosis of lupus is clinical, but some laboratory studies are essential to rule in or rule out renal or hematologic abnormalities and determine the level of disease activity. Tests usually ordered in patients suspected of having lupus include antinuclear antibody, complement levels, a complete blood cell count and differential, and a urinalysis. The need for additional tests depends on the results of the tests listed.

Once the disease is diagnosed, treatment should be tailored to the severity and type of clinical manifestations present. In general, glucocorticoids should be used at the smallest possible dose, antimalarials should be prescribed from the outset to all patients (following current guidelines in order to avoid ocular toxicity),[33] and immunosuppressants and other treatments should be considered in certain instances. In parallel, consideration should be given to sun protection, adequate exercise, tobacco avoidance, osteoporosis and atherosclerosis prevention, planned conception, and compliance.

The goal in these people at risk is to control their lupus manifestations without causing undue damage, to preserve their quality of life, and to prevent an early demise.

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