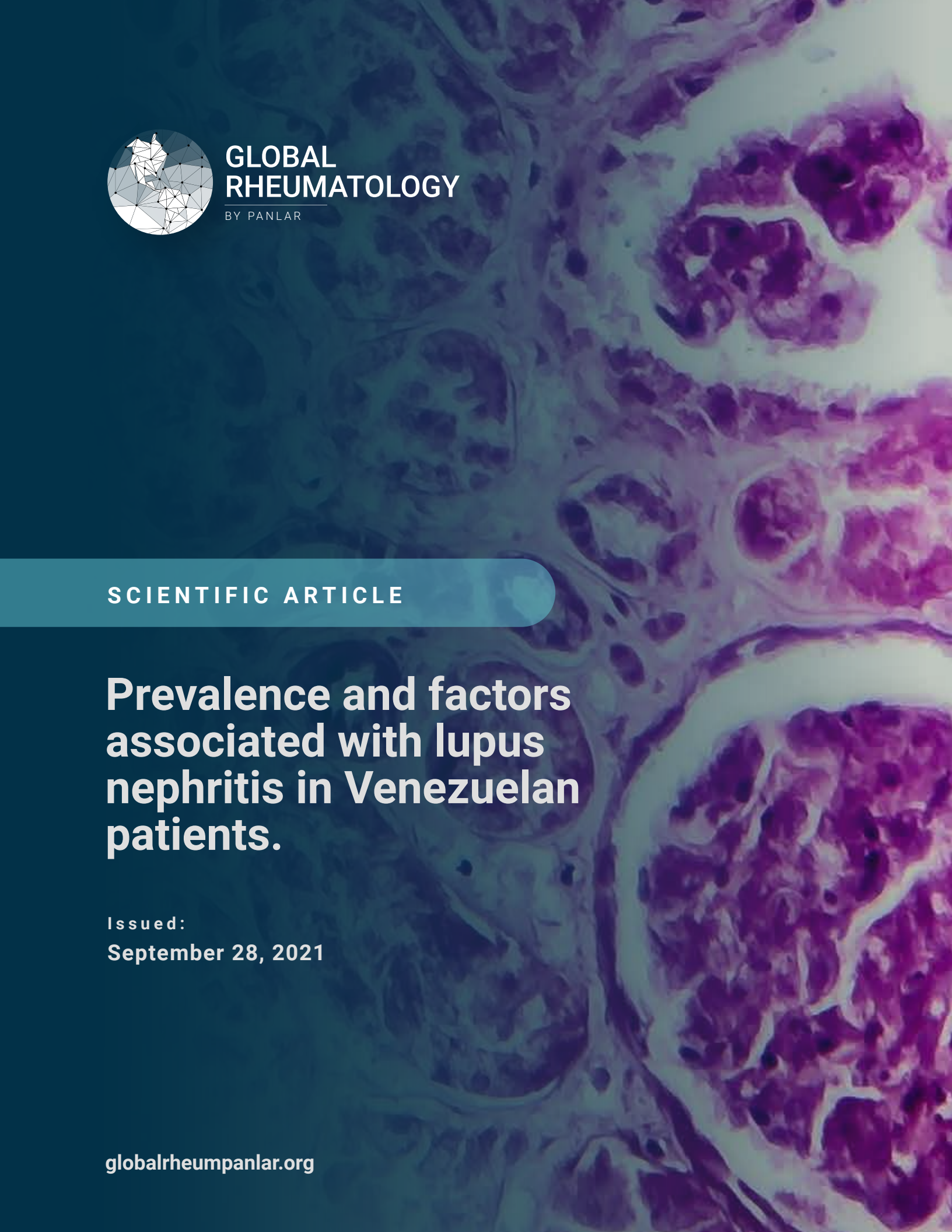

GLOBAL RHEUMATOLOGY
BY PANLAR

SCIENTIFIC ARTICLE

Prevalence and factors associated with lupus nephritis in Venezuelan patients.

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GLOBAL RHEUMATOLOGY
BY PANLAR

SCIENTIFIC ARTICLE

Prevalence and factors associated with lupus nephritis in Venezuelan patients.

GLOBAL RHEUMATOLOGY
BY PANLAR

Abstract
in English

Introduction / Objective
There are scarce data on lupus nephritis from single Latin American countries. We have assessed the prevalence and factors associated with lupus nephritis in a sample of Venezuelan patients with systemic lupus erythematosus.

Methods
A cross-sectional study of 406 SLE patients from a tertiary center in Caracas classified using the 1982 American College of Rheumatology criteria. Measures included sociodemographic, smoking, alcohol consumption, clinical features, treatment, and immunologic tests. Lupus nephritis defined as persistent proteinuria ≥ 0.5 g per day, an active urinary sediment plus an immunological feature, either hypocomplementemia or anti-dsDNA antibodies. Logistic regression analysis used to estimate the odds ratio (OR) of the factors associated with lupus nephritis.

Results
Thirty-three percent of patients were classified as having lupus nephritis. Logistic regression analysis showed that for each one-year increase in age the OR of having lupus nephritis is 0.97 (95% CI, 0.95 -0.98) and for each one-year increase in disease duration the OR of having lupus nephritis is 0.96 (95% CI, 0.94 -0.99). Current alcohol drinking, concurrent lupus disease activity and accrued organ damage were significantly associated with lupus nephritis.

Conclusion
Lupus nephritis was associated with lower age and shorter disease duration. Despite being a high-risk race/ethnic population and in a geographical region of high prevalence, Venezuelan patients showed a lower proportion of lupus nephritis closer to that of patients of European descent, suggesting that renal disease expression may not be uniform and may vary within individual Latin American countries despite sharing a common race/ethnicity and geography.

GLOBAL RHEUMATOLOGY
BY PANLAR

Abstract
in Spanish

Introducción / Objetivo
Hay escasos datos sobre la nefritis lúpica en países individuales de América Latina. Hemos evaluado prevalencia y factores asociados a la nefritis lúpica en pacientes venezolanos con lupus eritematoso sistémico.

Métodos
A cross-sectional study of 406 SLE patients from Estudio transversal de 406 pacientes con LES (criterios del American College of Rheumatology 1982). Nefritis lúpica definida como proteinuria persistente ≥ 0,5 g, sedimento urinario activo más hipocomplementemia o anticuerpos anti-dsDNA. Análisis de regresión logística para estimar la razón de probabilidades (OR) de factores asociados con nefritis lúpica.

Resultados
Treinta y tres por ciento de pacientes fueron clasificados como nefritis lúpica. El análisis de regresión logística mostró que por cada aumento de un año en la edad, el OR de nefritis lúpica es 0,97 (IC del 95%, 0,95 a 0,98), y por cada aumento de un año en la duración de la enfermedad el OR es 0,96 (95% % IC, 0,94 -0,99). El consumo de alcohol, la actividad de la enfermedad y el daño orgánico se asociaron con nefritis lúpica.

Conclusión
La nefritis lúpica se asoció con menor edad y menor duración de la enfermedad. A pesar de ser una población racial / étnica de alto riesgo y en una región geográfica de alta prevalencia, los pacientes venezolanos mostraron una menor proporción de nefritis lúpica y más cercana a la de los pacientes de ascendencia europea, lo que sugiere que la expresión de la enfermedad renal puede variar dentro de países latinoamericanos individuales que comparten una raza / etnia y geografía comunes

Abstract
in Portuguese

Introdução / Objetivo
Existem poucos dados sobre nefrite lúpica em alguns países da América Latina. Avaliamos a prevalência e os fatores associados à nefrite lúpica em uma amostra de pacientes venezuelanos com lúpus eritematoso sistêmico.

Métodos
Estudo transversal de 406 pacientes com LES de um centro terciário em Caracas (critérios do American College of Rheumatology de 1982). As medidas incluíram sociodemográficas, tabagismo, álcool, características clínicas, tratamento e testes imunológicos. Nefrite lúpica definida como proteinúria persistente ≥ 0,5 g por dia, sedimento urinário ativo mais hipocomplementemia ou anticorpos anti-dsDNA. Análise de regressão logística usada para estimar o odds ratio (OR) dos fatores associados à nefrite lúpica.

Resultados
Trinta e três por cento dos pacientes foram classificados como nefrite lúpica. A análise de regressão logística mostrou que para cada aumento de um ano na idade, o OR de nefrite lúpica é 0,97 (IC 95%, 0,95 -0,98) e para cada aumento de um ano na duração da doença, o OR de nefrite lúpica é de 0,96 (95 % CI, 0,94 -0,99). O consumo de álcool, a atividade da doença e os danos acumulados foram associados à nefrite lúpica.

Conclusão
A nefrite lúpica foi associada a menor idade e menor duração da doença. Apesar de ser uma população de raça / etnia de alto risco e em uma região geográfica de alta prevalência, os pacientes venezuelanos apresentaram uma proporção menor de nefrite lúpica mais próxima da de pacientes de ascendência europeia, sugerindo que a expressão da doença renal pode variar dentro países latino-americanos individuais.

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease affecting predominantly young women all over the world (1). It is characterized by loss of tolerance to autoantigens that leads to a chronic inflammatory response, driven by the intertwined participation of the innate and adaptive branches of the immune system, potentially affecting multiple organs and systems (2). The prevalence and severity of the disease varies as a function of race, ethnicity, socioeconomic status (SES), and geographical region (1). People of African descent have the highest incidence and prevalence (1, 3, 4). The Latin America mestizo population is an admixture of European, African American, and Amerindian cultural and genetic makeup, in proportions that vary among regions and even within specific countries (5). Patients from Latin America show a prevalence of renal lupus intermediate between those of African American and Caucasian populations (1). In Venezuela, the prevalence of SLE has been estimated at 70/100000 (1,6). Patients of African American and Hispanic heritage are known to be affected more seriously for reasons related to, but not exclusively determined, by SES factors (7,8). The Grupo Latinoamericano de Estudio del Lupus (GLADEL) study, a multinational cohort of 1214 patients with SLE in 9 Latin American countries (9), found that Mestizo and African American patients had more severe disease, including higher frequency of renal lupus, compared to Latin American whites (10). Similar results were previously reported in the LUpus in Minorities: Nature versus nurture (LUMINA) study, a multi-ethnic study including Hispanic patients residing in the US (11).

Lupus nephritis (LN) is one of the most common and serious manifestation in patients with SLE. The prevalence of nephritis in SLE varies greatly by race and ethnicity (12). Latin America is an area covering an extensive geographical region with a population sharing several phenotypic, ethnic, and cultural characteristics. However, ethnic/race mixing has not occurred to the same degree in the region, leading to variable genetic substructures potentially affecting disease expression in individual Latin American countries (13). For instance, Argentinians bear 80%, 18%, and 2% European, Amerindian, and African stock, respectively (14). Mestizo populations from Peru show a distinctive Native American ancestry signature (15), Puerto Rico and Colombia have higher levels of European as compared to Native American ancestry genes than mestizo populations from Mexico and Peru (16). The majority of the Venezuelan mestizo population now live predominantly in urban areas and, according to analysis using autosomal, Y-chromosome, and mtDNA markers, show a predominance of an European genetic component (40-65%), followed by Amerindian (20-35%) and African (10-20%) (17). This heterogeneous genetic substructure, as well as the influence of local

environmental factors related to sociocultural differences throughout the extensive Latin American region, may influence the risk for disease and disease clinical expression between countries. For example, Native American ancestry affected the prevalence of respiratory variables in admixed Mexican individuals (16). The objective of this study was to establish the prevalence and identify factors associated with LN in a sample of Venezuelan patients with SLE. We hypothesized that, given their genetic substructure and environmental background, Venezuelan lupus patients may show distinctive clinical characteristics, including target-organ disease expression, as compared to those reported in other Latin American patient populations.

Materials And Methods

Study design

This was an observational, cross-sectional study of 406 consecutive patients seen at the Division of Rheumatology, Hospital Universitario de Caracas, Venezuela, during the period 2013 to 2017.

Patient population and clinical assessment

Patients who were ≥ 18 years old were classified as having SLE if 4 or more criteria of the 1982 American College of Rheumatology (ACR) definition were present (18). All patients were interviewed and examined at the time of recruitment, following a detailed protocol to collect information on sociodemographic, clinical, and laboratory features at the time of enrollment. The study was approved by the Bioethics Committee of the Hospital Universitario de Caracas (protocol # 24/2013) and all subjects provided written informed consent to participate.

Socio-demographics

Age, gender, years of formal education, and marital status data were collected. SES was established using the modified Graffar scale (19) comprising five categories from 1 to 5 in decreasing order of SES level. These were collapsed into three variables, leaving a Graffar SES scale ranging from 1 to 3, where level 3 corresponds to the poverty level.

Clinical features

Disease duration, age at onset, clinical and laboratory data, family lupus history, comorbidities (hypertension, dyslipidemia, and diabetes mellitus), body mass index (BMI: weight in kilograms divided by height in squared meters), and treatment modality were collected. Disease activity at the time of the interview was assessed by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) (20); a cut-off value of ≥ 6 was used to define active disease. Damage accrual was assessed at the time of the interview using the Systemic

Lupus International Collaborating Clinics American College of Rheumatology (SLICC) Damage Index (DI) (21) as a binary (No =0, YES= >0) or continuous variable.

Classification into the neurolupus subset was done if the patient presented at least one of the corresponding components of the ACR criteria for neuropsychiatric manifestations, divided into central and peripheral components (22). Classification into the mucocutaneous (skin manifestations and oral ulcers) and hematologic subsets was done if patients fulfilled at least one of the corresponding components of the 1982 ACR criteria for SLE at the time of recruitment.

Lab tests corresponded to the period within the three months before inclusion in the study. Estimated glomerular filtration rate (eGFR) was calculated in ml per minute per 1.73 m2. Antinuclear antibodies (ANA) were tested by indirect immunofluorescence in Hep-2 cells; anti-dsDNA antibodies were tested by the Crithidia lucillae immunofluorescent test (CLIFT); lupus anticoagulant was measured by the dilute Russell Viper Venom Time and activated partial thromboplastin time (APPT); all other autoantibodies were detected by commercially available enzyme-linked immunosorbent assays. The positivity of an immunological test was established by the patient having at least two positive test results at least six months apart during the course of the disease. Low C3 and low C4 were defined as a value of < 60 mg/dL and < 15 mg/dL, respectively.

LN was established if the patient fulfilled the revised ACR criteria for LN, consisting of persistent proteinuria ≥ 0.5 g per day plus an active urinary sediment, and an additional third immunological feature, either hypocomplementemia or the presence of anti-dsDNA antibodies (23). Exclusion criteria for classification in the renal lupus subset included renal lithiasis (N = 25), hydronephrosis (N = 2), polycystic renal disease (N = 2), and history of renal cancer (N = 1), leaving a total of 376 patients. An additional 23 patients had insufficient urinary laboratory data for classification, leaving a final total of 353 patients for analysis in the renal lupus subset.

Statistical analysis

Descriptive statistics included means or medians with standard deviations and interquartile ranges, respectively. T-test and chi-square tests were used to test the differences between sociodemographic and clinical features by the presence of renal disease. Logistic regression analysis was performed to test the association with LN of sociodemographic characteristics, current smokers, current drinkers, comorbidities, laboratory, and clinical features. Statistical significance was set at $p < 0.05$. Analyses were conducted using the Stata15 package (StataCorp. LLC, Stata Statistical Software: Release 15. College Station, TX).

Results

Sample population, sociodemographic features, and health lifestyle

The sample included a total of 406 patients. The mean age was 41.0 ± 12.2 years, female sex was 95%, Hispanic ethnicity was 98%, mean years of education was 11.9 ± 4.0; most patients were single (48%), and 29% were classified in the poverty Graffar SES level 3 (Table 1).

Clinical features

Mean disease duration was 10.0 ± 8.2 years; age at disease onset was 30.9 ± 11.3 years. The most common cumulated 1982 ACR criteria at the time of inclusion were arthritis (89%), malar rash (60%), photosensitivity (57%), renal disease (43%), oral ulcers (42%), and hematologic disorder (40%). Mucocutaneous, hematological, and neurolupus lupus were seen in 87%, 40%, and 14% of patients, respectively. The mean SLEDAI score was 5.2 ± 5.6, and the proportion of clinically active patients at inclusion into the study (SLEDAI ≥ 6) was 41%; the mean SLICC DI was 0.8 ± 1.4 and 43% of patients scored a SLICC DI > 0. At the time of the study, 94% of patients were taking oral prednisone; anti-malarials, mycophenolate mofetil, and azathioprine were being taken by 77%, 23%, and 21% of patients, respectively (Table 1).

ANA was positive in 97% of cases, followed by anti-DNA (51%), anti-Sm (35%), anti-Ro (35%), anti-RNP (23%), and anti-La (17%) antibodies. Anti-phospholipid antibodies were observed in 23% of cases. Mean serum C3 and C4 levels were 75.8 ± 42.7 mg/dL and 20.6 ± 12.1 mg/dL, respectively.

Lupus nephritis

Of the 353 patients with complete data for renal disease analysis, 117 (33%) were classified as having LN at study entry. The mean creatinine clearance was 106.1 ± 51.8 ml/min, the mean eGFR was 101.6 ± 38.4 ml/min/1.73 m2 of body surface area, and the median 24-hour urinary protein excretion was 0.18 g (Interquartile range 75-25, 0.08-0.42). A renal biopsy performed in 65 patients showed the highest frequency in class II (27.6%), followed by class IV (21.5%), class I (20.0%), class V (16.9%), and class III (13.85%). In the total patient population, 24 patients (5.9%) had persistent 24-hour proteinuria > 3.5 g and 8 (1.9%) had end-stage renal disease.

Compared to those without renal lupus, patients with renal lupus were significantly more likely to be younger [38.4 vs 42.6 years (mean ± Standard Deviation, p-value = 0.001)], to be current alcohol drinkers (33%), to have shorter disease duration, to ever have anti-DNA antibodies, to have concurrent disease activity, to have accrued organ damage, and to have ever received intravenous pulses of cyclophosphamide or methyl prednisolone (Table 2).

Logistic regression analysis showed a 2.8% and 3.0% decrease in LN for each one-year increase in age and for each one-year increase in disease duration, respectively (Table 3). Current alcohol drinking (OR=1.64, 95% CI=1.00-2.68), ever having anti-dsDNA (OR=30, 95% CI=14.7-61.3), SLEDAI ≥ 6 (OR=4.95, 95% CI=3.06-8.03), and SLICC DI > 0 (OR=2.32, 95% CI=1.46-3.69) were factors independently associated with renal lupus.

Discussion

We examined the prevalence of LN and associated factors in Venezuelan patients with SLE from a tertiary center in Caracas. We found that the prevalence of LN was lower than expected and greater in younger patients and those with a shorter disease duration. Alcohol drinking, ever having anti-dsDNA antibodies, disease activity, and accrued organ damage were also associated with LN.

Female sex predominated in a proportion of 9/1 as seen worldwide (1, 24), and similar to that previously reported in Hispanic patients (25). The mean age at disease onset in our patients was within the 15-to-45 years bracket, as is typical for SLE populations worldwide (1) and in Hispanic patients (8, 9). Mean years of education was comparable to findings in the Latin American GLADEL and the mestizo LUMINA subset. A lower proportion of our patients, 29% vs. 63% in the GLADEL mestizo subset (9) and 39% in the mestizo LUMINA subset (11), were classified in the SES level of poverty. Our frequency of current smokers, those with comorbid diabetes, and mean BMI were comparable to those from the SLICC multiracial and multinational series (26).

The distribution of clinical manifestations in our series was comparable to that of a large national registry of Spanish lupus patients (27) and the GLADEL and PROFILE cohorts (9, 28), except for more frequent hematological manifestations and renal disease in the latter two. Musculoskeletal symptoms are the most prevalent manifestation of SLE, affecting up to 95% of patients, followed by mucocutaneous symptoms (9, 27-31). Serositis, as well as renal and neurological manifestations, prevail in African American patients (1). Progress to end-stage renal disease occurs more frequently among African American (1, 32) and Hispanic patients (33). Interestingly, LN was seen in a lower proportion of our patients (33%) as compared to the PROFILE Hispanic subset (59%) (28) and the GLADEL (52%) cohort (9), and closer to the proportion of 34% in white patients of the Spanish SLE national registry (27), 31.9% of those in the Michigan Registry (29), and 39.5% of those in the California Lupus Surveillance Project (30). It is possible that the more stringent criteria used to define renal disease in our study, including the need for an immunological criterion of disease activity (the presence of either anti-DNA or low complement values) (23), can account for these differences. However, even when using the original, less stringent, 1982 ACR criteria for renal disease,

the proportion of our patients with LN was 43%, still lower than that described in those other Hispanic cohorts.

European ancestry genes are known to protect against renal disease in lupus patients (1, 9, 28, 34-36). Thus, it is possible that the genetic substructure of our patient population, with a relatively high component of European stock (17), may partially explain these findings. The most recent immigration wave from Europe to Venezuela after World War II further contributed to this genetic component, after previous successive waves from Spain, Germany, and Corsica in the colonial and post-colonial past (17).

It is worth observing that, in the limited subsample of our patients with renal biopsy (N = 65), only 21% had type IV glomerulonephritis, the most aggressive form of lupus nephropathy; furthermore, only 6% of our total patient population sample had persistent nephrotic-range proteinuria and only 2% had reached an end-stage renal disease level at inclusion in the study. We cannot rule out a biased selection of patients for renal biopsy, from those with less firm clinical evidence of LN as opposed to those with overt renal disease, as an explanation for the lower proportion of patients with the most severe forms of LN. Compared to the LUMINA Hispanic subset and the GLADEL mestizo subset, a relatively lower proportion of our patients (29%) were classified at the SES level of poverty, another variable associated with increased risk for renal disease (37-39). However, as also seen in a multi-ethnic lupus study (36), we found no effect of SES level on predisposition to renal disease, possibly explained by the cross-sectional design of our study. In addition, data from the LUMINA study support the notion of genetic factors prevailing over SES level in susceptibility to renal disease (11).

Lower mean age and shorter disease duration were associated with increased frequency of LN, as previously reported in Hispanic patients (1, 10 39). The relationship between alcohol and risk of lupus has been a controversial subject, with one study showing a moderate protective effect (40) and another showing none (41).

Clinical disease activity and accrued organ damage correlated with the presence of LN in our study, consonant with previous reports (8, 20, 42, 43). However, a lower proportion of our patients (43%) accrued tissue damage compared to Hispanics and Afro-Americans in the LUMINA cohort (61% and 51%, respectively).

Limitations of our study are its cross-sectional design, which may veil the role of sociodemographic and clinical factors in conferring the risk of LN over time; the site of the study in a tertiary referral hospital, limiting its generalizability; and the low proportion of patients with histological confirmation of LN. Its strengths are the racial/ethnic homogeneity of the patient population; its single-country

nature testing the specificities of cultural and genetic factor interactions within a common population; and the location of Venezuela in the Caribbean, a known high-risk area for LN as a test for the influence of ambience.

In summary, the prevalence of LN was lower than expected for an Hispanic SLE population. Independent factors associated with lupus renal disease were age, disease duration, current alcohol drinking, ever having anti-DNA antibodies, lupus disease activity, and accrued tissue damage. The lower frequency of renal disease observed in Venezuelan patients, as compared to other Hispanic lupus populations, underscores the need to examine differences in the clinical expression of SLE within individual Latin American countries.

Table 1. Sociodemographic and clinical features of Venezuelan SLE cohort (n = 406).

Variable	N (%)
Age (years) mean ± SD 41.0 ± 12.2	41.0 ± 12.2
Female sex 385 (94.83)	385 (94.83)
Hispanic ethnicity 386 (97.72)	386 (97.72)
Years of education m ± SD 11.9 ± 4.0	11.9 ± 4.0
Marital status	
Single	196 (48.28)
Married	106 (26.11)
Partner	72 (17.73)
Widowed	11 (2.71)
Divorced	21 (5.7)
Graffar SES	
1 (upper, upper middle)	35 (9.02)
2 (middle)	241 (62.11)
3 (poverty)	112 (28.87)
Current cigarette smoking 60 (14.89)	60 (14.89)
Current alcohol consumption	113 (27.90)
Disease duration (years), mean ± SD	10.05 ± 8.2
Age at disease onset (years), mean ± SD	30.9 ± 11.3
Family history of lupus	72 (18.41)
Hypertension	169 (41.94)
Dyslipidemia	101 (25.06)
Diabetes mellitus 9 (2,23)	9 (2,23)
1982 ACR criteria	
Malar rash	242 (59.61)
Discoid lupus	73 (18.07)
Photosensitivity	230 (56.79)
Oral ulcers	170 (41.98)
Arthritis	363 (89.41)
Serositis	105 (25.86)
Renal disease*	168 (43.08)
Neurologic disorder	33 (8.42)
Hematologic disorder	163 (40.45)
Immunologic disorder	319 (78.57)
Antinuclear antibody	397 (98.27)

Variable	N (%)
Total number ACR criteria (median, 25%-75% IQR)	5 (5-7)
Lupus subsets	
Lupus nephritis ¶ (n = 353)	117 (33.05)
Neurological § (n = 394)	52 (13.61)
Mucocutaneous (n = 393)	342 (86.80)
Hematological (n = 391)	158 (40.41)
SLEDAI score, mean ± SD	5.22 ± 5.6
SLEDAI active patients *	162 (41.01)
SLICC damage, index mean ± SD	0.87 ± 1.41
Current treatment	
Oral prednisone	380 (93.6)
Anti-malarials	309 (77.0)
Mofetil mycophenolate	94 (23.4)
Azathioprine	84 (20.9)
NSAID	31 (7.8)
Methotrexate	29 (7.2)
Cyclophosphamide E.V. pulses	19 (4.7)
Methyl prednisolone E.V. pulses	15 (3.7)
Rituximab	5 (1.2)

Note: SLEDAI cut-off for activity ≥ 6; ACR= American College of Rheumatology; NSAID= Non-steroidal Anti-Inflammatory Drugs; SES= socioeconomic status; SLE= Systemic lupus erythematosus; SLEDAI= Systemic Lupus Erythematosus Disease Activity index; SLICC= Systemic International Collaborating Clinics.

* Applying the 1982 ACR criteria for SLE classification.
¶ Applying the modified ACR criteria for renal lupus (Dooley et al).
§ Applying the ACR Ad Hoc Committee on neuropsychiatric lupus nomenclature.

Table 2. Sociodemographic and clinical features in patients by lupus nephritis (N = 353).

Variable	Lupus nephritis		
	Yes N (%)	No (%)	p-value
Total	117 (33.0)	236 (66.8)	
Age (years) men ± SD	38.41 ± 12.37	42.66 ± 12.07	0.001¶
Female sex	109 (93.16)	228 (96.20)	0.208
Education (years) mean ± SD	11.93 ± 3.81	11.88 ± 3.94	0.5406
Graffar SES			
1	7 (6.14)	26 (11.06)	
2	77 (67.54)	139 (59.15)	
3	30 (26.32)	70 (29.79)	0.205
Marital status			
Single	60 (51.28)	120 (50.63)	
Married/partner	50 (42.74)	96 (40.51)	
Widowed	3 (2.56)	6 (2.53)	
Divorced	4 (3.42)	15 (6.33)	0.720
Family lupus	23 (19.66)	38 (16.24)	0.426
Current cigarette smoking	20 (17.09)	28 (11.97)	0.187
Current alcohol drinking	39 (33.33)	55 (23.31)	0.045
Disease duration (yrs.), mean ± SD	8.80 ± 7.39	10.75 ± 8.46	0.017¶
BMI (Kg/m2), mean ± SD	25.03 ± 4.40	25.58 ± 5.15	0.1685
Hypertension	51 (43.59)	94 (40.17)	0.540
Diabetes	3 (2.56)	5 (2.13)	0.796
Dislipidemia	30 (25.86)	57 (24.26)	0.743
Neurolupus	22 (19.82)	28 (12.12)	0.059
Mucocutaneous Lupus	107 (91.45)	202 (85.23)	0.098
Hematological lupus	45 (38.79)	101 (42.62)	0.493
Clinical activity (SLEDAI > 6).	77 (66.96)	67 (29.00)	0.000
Organ damage (SLICC DI >0)	64 (57.14)	82 (36.44)	0.000
Anti-DNA ever	105 (91.30)	61 (25.85)	0.000
Anti-Sm ever	44 (43.56)	73 (33.18)	0.073
Anti-RNP ever	22 (24.18)	48 (24.24)	0.990
Anti-Ro ever	40 (42.11)	65 (31.40)	0.070
Anti-La ever	20 (23.53)	30 (15.15)	0.090
ACA IgG ever	16 (17.39)	24 (12.77)	0.299
ACA IgM ever	9 (9.89)	16 (8.47)	0.695

Table 2. Sociodemographic and clinical features in patients by lupus nephritis (N = 353).

Variable		Lupus nephritis	
Anti-β2 GPI IgG	3 (3.45)	7 (3.83)	0.878
Anti-β2 GPI IgM	11 (12.94)	14 (7.73)	0.175
Lupus inhibitor*	2 (2.94)	7 (4.96)	0.500
Current use anti-malarials	92 (78.63)	183 (78.54)	0.984
Current use azathioprine	26 (22.22)	52 (22.22)	1.000
Current use methotrexate	6 (5.13)	17 (7.30)	0.440
Current use MMF	30 (25.64)	51 (21.89)	0.432
Current use oral cyclophosphamide	8 (6.84)	9 (3.85)	0.218
Ever use methylprednisolone pulses	45 (38.46)	59 (25.11)	0.010
Ever use cyclophosphamide pulses	41 (35.04)	57 (24.66)	0.033

Statistical analysis by Pearson Chi square test. ¶ Unpaired Student's t test

*lupus inhibitor (N = 209); anti-malarials = hydroxychloroquine or chloroquine; BMI=body mass index; DI= damage index; MMF= mycophenolate mofetil; SLEDAI= Systemic Lupus Erythematosus Activity Index; SLICC= Systemic Lupus International Collaborating Clinics Classification Criteria for Systemic Lupus Erythematosus; SES=socioeconomic status.

Table 3. Multivariate logistic regression analysis for lupus nephritis among Venezuelan patients with SLE (n = 353).

Variable	OR	95% CI	p-value
Age	0.97	0.95 0.98	0.002
Female sex	0.53	0.20 1.43	0.215
Civil status			
Single	Reference		
Married	0.74	0.37 1.50	0.416
Partner	1.00	0.16 5.90	1.000
Widow	1.68	0.78 3.58	0.178
Divorced	0.45	0.10 1.90	0.282
Graffar SES			
Upper, upper middle	Reference		
Middle	1.38	0.62 3.04	0.424
Poverty	0.90	0.37 2.18	0.817
Family history	1.26	0.71 2.23	0.426
Disease duration	0.96	0.94 0.99	0.037
Years of education	1.00	0.94 1.06	0.918
BMI	0.97	0.93 1.02	0.337
Cigarette smoking	1.51	0.81 2.82	0.190
Current alcohol drinking	1.64	1.00 2.68	0.046
Hypertension	1.15	0.73 1.80	0.540
Diabetes	1.21	0.28 5.15	0.796
Dislipidemia	1.08	0.65 1.81	0.743
Neurolupus	2.60	0.68 9.87	0.160
Mucocutaneous lupus	1.85	0.88 3.88	0.102
Hematological lupus	0.85	0.54 1.34	0.493
SLEDAI ≥ 6	4.95	3.06 8.026	0.000
SLICC DI (>0)	2.32	1.46 3.69	0.000
Anti-DNA ever	30.12	14.79 61.33	0.000
Anti-Sm	1.55	0.95 2.52	0.074
Anti-RNP	0.99	0.55 1.77	0.990
Anti-Ro	1.58	0.96 2.62	0.071
Anti-La	1.72	0.91 3.24	0.093
Anti-cardiolipin IgG	1.43	0.72 2.86	0.301
Anti-cardiolipin IgM	1.18	0.50 2.79	0.696
Anti-β2 GPI IgG	0.89	0.22 3.55	0.878-

Table 3. Multivariate logistic regression analysis for lupus nephritis among Venezuelan patients with SLE (n = 353).

Variable	OR	95% CI	p-value
Anti-β2 GPI IgM	1.77	0.76 4.09	0.179
Anti-malarials	1.00	0.58 1.72	0.984
Azathioprine	1.00	0.58 1.70	1.000
Methotrexate	0.68	0.26 1.79	0.442
Mofetil mycophenolate	1.23	0.73 2.06	0.433
Cyclophosphamide	1.88	0.68 4.88	0.225

(LR chi2 = 9.56, p = 0.0020)

Note: SES= socioeconomic status; BMI= body mass index; MMF= mycophenolate mofetil; SLEDAI= Systemic Lupus Erythematosus Activity Index; SLICC= Systemic Lupus International Collaborating Clinics Classification Criteria for Systemic Lupus Erythematosus; DI= damage index.

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