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Clinical and immunohistopathological correlation of lupus nephropathy in a reference center of the Colombian Caribbean during the years 2012 to 2013

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ABSTRACT

Objectives: To determine the behavior of lupus nephropathy (LN) in a population group of a reference center in the Colombian Caribbean during 2012 and 2013, analyzing the most prevalent clinical and laboratory findings and its relation to the immunohistotopathological findings, define the class of Lupus nephritis with greater prevalence and the clinical or paraclinic data more correlated with this one.

Methods: Descriptive, retrospective, cross-sectional study conducted from January 1st of 2012 to December 31st 2013, which included 53 patients with systemic lupus erythematosus according to diagnostic critearia of the Colegio Americano de Reumatologia, with manifestations of renal impairment.

Results: In our study population in the Colombian Caribbean, LN predominates more in women and class IV represents 66.03% of the total cases analyzed, in which there was more hematuria present, hypertension and proteinuria with nephrotic pattern, as well as higher levels of serum creatinine. Despite the lack of data, none of the clinical or paraclinical variables was specific for a certain class of LN and in relation to the immunostaining, lambda chains were positive in 100% of the cases and only C4 and fibrinogen were specific to LN class IV.

Conclusions: Class IV LN is the most prevalent and with a higher percentage of predominance of the variables hematuria, proteinuria, hypertension, elevated serum creatinine and bun levels. At the same time they are not specific for some class of LN in our population.

Key Words: Lupic Nephropathy, Histopathology.

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Correlación clínica e inmunohistopatológica de la nefropatía lúpica en un centro de referencia del Caribe colombiano durante los años 2012 a 2013

RESUMEN

Objetivos: Determinar el comportamiento de la nefropatía lúpica (NL) en un grupo poblacional de un centro de referencia del Caribe colombiano, durante los años 2012 y 2013, analizando los hallazgos clínicos y de laboratorio más prevalentes y su relación con los hallazgos inmunohistopatológicos, definir la clase de NL con mayor prevalencia y el dato clínico o paraclínico más correlacionado con esta.

Métodos: Estudio descriptivo, retrospectivo, transversal, realizado desde el 1 de enero de 2012 al 31 de diciembre de 2013, que incluyó a 53 pacientes con lupus eritematoso sistémico (LES), según los criterios diagnósticos del Colegio Americano de Reumatología, con manifestaciones de compromiso renal.

Resultados: En nuestra población de estudio del Caribe colombiano, la NL predomina más en mujeres y la clase IV representa el 66,03% del total de casos analizados, en los cuales hubo más presentación de hematuria,hipertensión y proteinuria con patrón nefrótico, al igual que mayores niveles de creatinina sérica. A pesar de la falta de datos, ninguna de las variables clínicas o paraclínicas fue específica para cierta clase de NL y con relación a la inmunomarcación, las cadenas lambda se presentaron positivas en el 100% de los casos y tan solo el C4 y el fibrinógeno fueron específicos de la NL clase IV.

Conclusiones: La NL clase IV es la más prevalente y con mayor porcentaje de predominio de las variables como hematuria, proteinuria, hipertensión, niveles de creatinina y BUN séricos elevados y, a su vez, no son específicos para cierta clase de NL en nuestra población.

Palabras clave: Nefritis lúpica, Histopatología.

INTRODUCTION

Renal impairment in patients with systemic lupus erythematosus (SLE) is very high in relation to the involvement of other organs. Literature supports that, up to 50% of these patients can present with lupus nephritis (LN) with an incidence of up to 55% in Asians of 51% in Africans, 43% in Hispanics and 14% In Caucasians, according to their demographic characteristics. [1, 2]

Studies in the European population establish that renal impairment as the first manifestation of SLE comes in second place in young population in relation to the elder, in which it becomes less frequent. [3] Likewise underage is considered a risk factor for severe lupus nephritis (SLN).

Regarding gender and socio-demographic characteristics, there are retrospective studies in the American population that establish that the prevalence of LN is 4 times higher in females than in males, [4] times higher among African Americans than in whites[4], and that young American males of European lineage are less likely to develop LN. [1]

Nearly half of the patients with LN manifest symptoms or paraclinical findings of kidney disease, with proteinuria being the most frequent, followed by active urinary sediment and elevated serum creatinine levels. Nevertheless, clinical manifestations underestimate the severity of renal involvement in the SLE patient, therefore we can find up to 15% of asymptomatic patients with LN class III, IV[5] (what we know as silent lupus nephritis). [6,7] In one Asian population study[8], it was established that clinical data such as proteinuria in nephrotic range were extrapolated and occurred in both proliferative and nonproliferative nephritis. There were cases of proteinuria in non-nephrotic ranges in almost 49% of proliferative LNs, which generates some indifference between the clinical correlation and the immunohistopathological findings in LN. This makes it necessary to perform a renal biopsy to define the ideal treatment and the forecast of the disease.

The nephritic syndrome can appear with or without renal failure and appears much more in membranoproliferative LN, and class V membranous, [9] being the nephritic syndrome the most characteristic of class IV LN.

From the pathophysiological point of view, in patients with class IV LN active, it's expected to present hematuria, proteinuria, with the consequent development of hypertension, nephritic syndrome and impaired renal function with low complement levels and elevated serum levels of anti DNA. Based on the classification of the International Society of Nephrology and Renal Pathology Society (ISN / RPS) for 2003, [10] 480 cases of LN in Japan were categorized, which results showed 3% with Class I, 16% Class II, 13% class III, 11% class IV-S, 41% class IV-G, 16% class V and 1% class IVG. Class IV-G was the highest incidence with end-stage renal disease[11], as published by Melvin Schwartz et al[12] in his reclassification work according to the ISN / RPS parameters.

Our research was conducted in a cohort of patients with LN in the Colombian Caribbean with the purpose of analyzing clinical and demographic variables; such as sex and age, and its correlation with the results of histopathology and immunostaining. Also to know its behavior in relation to other population groups, seeking to establish ideal guidelines for diagnosis, treatment and follow-up, in order to improve the forecast of our Patients with SLE and alleged renal disease.

MATERIALS AND METHODS

A retrospective and descriptive study was conducted during the years 2012 and 2013. Patients included were older than 18 with diagnosis of SLE and LN, admitted to the institution and in whose study of renal biopsy were not class overlap.

The diagnosis of SLE was made based on the diagnostic criteria of the American College of Reumathology[13] and the presence of LN was established due to hematuria (more than 5 erythrocytes per high power field) and persistent proteinuria greater than 0.5 g / Day in a patient with clinical deterioration and evidence of glomerulonephritis mediated by immune complexes compatible with LN on the renal biopsy. [14]

The study was carried out at Clínica de la Costa, an institution of 4th level of health care, located in the city of Barranquilla, Colombia. It is a reference center of patients with renal disease of the Colombian Caribbean.

The renal biopsies were interpreted by the nephrology department of the institution, according to ISN / RPS 2003. [10,16]

The data collection was done directly from the files of the department and the electronic medical records of each patient through the institution's clinical records software.

The variables analyzed were sex, age, clinical variables (blood pressure, hematuria), being classified from hypertension the findings of readings greater than 139 / 89mmhg, according to the seventh report of the national committee on prevention, detection, evaluation and treatment of hypertension arterial.

Hematuria in the active sediment was defined as the presence of 5 or more erythrocytes per field, according to the guidelines of treatment and management of LN of the American College of Reumathology. 24-hour proteinuria, serum creatinine, and serum Bun were all paraclinic variables. Immunological profile was analyzed (ANAS, C3, C4, anti-DNA, anti-SM, anti-LA, anti-RO), LN class, activity index and chronicity and immunofluorescence (IgA, IgG, IgM, C3, C4 , C1q, lambda, kappa, albumin and fibrinogen chains) and the deposition patterns of each immunomarker.

The Ethics Committee of the Health Sciences Division of the Universidad del Norte approved the study.

The statistical analysis was performed using the statistical software IBM-SPSS (Statistical Package for the Social Sciences) version 21.

RESULTS

During the period between January 2012 and December 2014, a total of 64 patients with LN were diagnosed. In five patients it was not possible to collect histopathological classification data (2 men and 3 women). Six patients appertained to class III / V overlap; all were female.

53 patients were analyzed with definitive diagnosis of lupus nephritis, distributed between classes II, III and IV (Table 1) (Graph 1).

The distribution by sex showed a higher frequency in women (90.5%) compared to men (9.5%). Class IV LN was the most frequent (66.03%), being higher in men (100%) than in women (62.5%). According to the age, LN featured more between the thirties and fourties. No class predominance was observed for this variable (Table 1).

In the class IV group, the frequency of arterial hypertension was of 70%, of elevated creatinine levels were 90%, of elevated serum BUN levels were 100%, of proteinuria in the nephritic range was 85%, and of hematuria was 80%, which was greater than in groups II and III (Table 1).

Of the immunomarkers, the most frequent was a lambda chain finding (100%), with a distribution between classes II, III and IV of 5.7%, 28.3% and 66% respectively; Followed by IgM (94.2%) with a distribution between classes II, III and IV, of 4.1%, 30.6% and 65.3%, respectively. IgG (92.4%) with a distribution between classes II, III, IV, of 6.1%, 26.5%, 67.3% respectively.

Fibrinogen and C4 scored positively 100% of the time only for LN class IV , followed by C1q (94.1%) and albumin (93.3%) (Table 2).

Hematuria was present in 86.77% of the cases, testing positive for IgA, IgG, IgM, C3, C4, C1q and lambda chains, with a standard deviation of 3.39; unlike patients which tested positive for Kappa chains where serum creatinine greater than 1.3 mg / dl represented the 83.9% and hematuria only 16.1% of all cases (Table 3).

Finally, ANAS, C3, C4, anti-DNA, anti-SM, anti-LA, anti-RO variables, which were part of the immunological profile, were not taken into account for their analysis due to a lack of data for each of them.

DISCUSSION

This study describes LN and the clinical and the histopathological correlation in a cohort of 54 patients

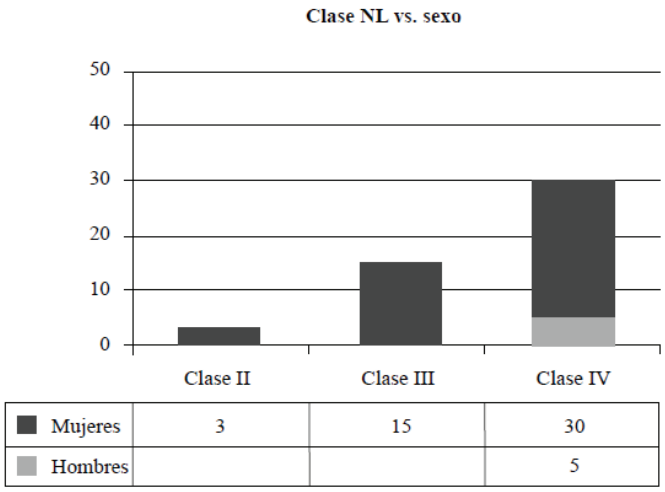
Table 1. Clinical and laboratory characteristics of patients with LN in a reference center of the Colombian Caribbean during the years 2012 to 2013

Characteristics		Histopathological Classification *		
		II III	I V	
Age years	m (DE)	36.67 (14.57)	30.27 (6.36)	32.66 (10.46)
Gender	Female	3 (6.3%)	15 (31.3%)	30 (62.5%)
	Male	0	0	5 (100%)
Hypertension	Negative	2 (6.7%)	9 (30%)	19 (63.3%)
	Positive	0	3 (30%)	7 (70%)
Creatinine	< 1.3mg/dl	2 (7.7%)	12 (46.2%)	12 (46.2%)
	≥ 1.3 mg/dl	1 (5%)	1 (5%)	18 (90%)
Proteinuria	< 3.5 gr	2 (8%)	11 (44%)	12 (48%)
	≥ 3.5 gr	0	0	13 (100%)
BUN	< 18 mg/dl	1 (5.6%)	10 (55.6%)	7 (38.9%)
	≥ 18 mg/dl	1 (5%)	2 (10%)	17 (85%)
Hematuria	Negative	0	1 (50%)	1 (50%)
	Positive	1 (3.3%)	5 (16.7%)	24 (80%)

*No patients with Histopathological Classification I, V or VI were found

Figure 1.

Prevalence of LN in the Colombian Caribbean according to gender and histopathological class.



from the Caribbean Region at Colombia. Women had more LN than men, and both young adults and the elder progressed the disease, which differs from other studies conducted in other populations where there were no significant differences in gender1, and from Data of the world literature that establish a higher prevalence of LN among men. [15]

According to the pathophysiology of the disease[12], the presence of hematuria and proteinuria in the urine test may be a bookmark of renal impairment due to SLE, although not very sensitive according to the scientific evidence5, therefore its absence underestimates in some chances the degree of renal compromise by autoimmunity. In this research we identified proteinuria as the most frequent finding, while values> = 3.5g / 24 hours were exclusive to class IV (Graph 2). The presence or absence of hematuria, arterial hypertension, serum creatinine> = 1.3mg / dl and BUN> = 18mg / dl were not index of a specific class of LN in the same way as a proteinuria <3.5gr / dl did not rule out a LN IV. This indicates that in our population the only way to establish the true degree of renal impairment is through the histopathological study of the renal biopsy and that the absence of hematuria, proteinuria, arterial hypertension, serum creatinine> = 1.3mg / dl and BUN> = 18mg / dl does not clinically rule out the presence of an LN.

In our study cohort, the female gender did not define a specific pattern of LN appearance and, although Class IV prevailed in 62.5%, there was also a distribution between II and III, unlike men in which they all presented the LN class IV. We can argue that the male sex would not protect against the high probability of suffering a LN class IV, but instead would behave as a higher risk factor.

Performing this study in a reference institution for the entire Colombian Caribbean, made it possible to have a sample that was significant, reflecting the behavior of lupus nephropathy in this area of the territory and the resulting knowledge be used to generate prevention and control strategies with relation to this enemy, that every day that passes, stops being hidden before medical science.

Among the limitations of the study it could be mentioned the size of the sample, however, as expressed previously, it can be considered that of our research, representative of the Caribbean Region of Colom-

Table 2. Immunostaining of patients with LN in a reference center of the Colombian Caribbean during the years 2012 to 2013

Characteristics		Histopathological Classification *		
		II	III	IV
IgA	Positive	1 (5.3%)	4 (21.1%)	14 (73.7%)
	Negative	2 (6.1%)	11 (33.3%)	20 (60.6%)
IgG	Positive	3 (6.1%)	13 (26.5%)	33 (67.3%)
	Negative	0	2 (50%)	2 (50%)
IgM	Positive	2 (4.1%)	15 (30.6%)	32 (65.3%)
	Negative	1 (33.3%)	0	2 (67.7%)
C3	Positive	0	13 (27.7%)	34 (72.3%)
	Negative	3 (50%)	2 (33.3%)	1 (16.7%)
C4	Positive	0	0	14 (100%)
	Negative	3 (7.7%)	15(38.5%)	21 (53.8%)
C1q	Positive	0	2 (5.9%)	32 (94.1%)
	Negative	3 (15.8%)	13 (68.4%)	3 (15.8%)
Lambda	Positive	3 (5.7%)	15 (28.3%)	35 (66%)
	Negative	0	0	0
Kappa	Positive	1 (2.2%)	11 (24.4%)	33 (73.3%)
	Negative	2 (25%)	4 (50%)	2 (25%)
Albumin	Positive	0	1 (6.7%)	14 (93.3%)
	Negative	3 (8.1%)	14 (37.8%)	20 (54.1%)
Fibrinogen	Positive	0	0	14 (100%)
	Negative	3 (7.9%)	15 (39.5%)	20 (52.6%)

bia. The retrospective collection of available information revealed the absence of other data, that could be evaluated together with those that are part of this research.

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Tabla 3. Clinical and laboratory characteristics in relation to the immunomarcation of patients with NL in a reference center of the Colombian Caribbean during the years 2012 to 2013

Characteristics		Hypertension		Creatinine (mg / dl)		Hematuria		Proteinuria (gr / dl)	
		Positive	Negative	<1.3	>=1.3	Positive	Negative	<3.5	>=3.5
IgA	Positive	3(16.7%)	15 (83.3%)	8 (44.4%)	10 (55.6%)	14 (93.3%)	1 (6.7%)	9 (64.3%)	5 (35.7%)
	Negative	6(23.1%)	20 (76.9%)	23(65.7%)	12 (34.3%)	18 (81.8%)	4 (18.2%)	17 (58.6%)	12 (42.44%)
IgG	Positive	9(20.9%)	34(79.1%)	29 (58%)	21 (48%)	31 (86.1%)	5 (13.9%)	25 (58.1%)	18 (41.9%)
	Negative	1(33.3%)	2(66.7%)	2 (50%)	2 (50%)	3 (100%)	0	0	2 (100%)
IgM	Positive	9(21.4%)	33(78.6%)	30(58.8%)	21(41.1%)	31(86.1%)	5(13.9%)	26(61.9%)	16(38.1%)
	Negative	1(33.3%)	2(66.6%)	1(33.3%)	2(66.7%)	2(100%)	0	1(50%)	1(50%)
C3	Positive	10(25%)	30(75%)	26(55.3%)	21(44.7%)	31(88.6%)	4(11.4%)	24(60%)	16(40%)
	Negative	0	5(100%)	5(71.4%)	2(28.6%)	2(66.7%)	1(33.3%)	3(75%)	1(25%)
C4	Positive	5(35.7%)	9(64.3%)	4(28.6%)	10(71.4%)	10(83.3%)	2(16.7%)	7(58.3%)	5(41.7%)
	Negative	5(16.1%)	26(83.9%)	27(67.5%)	13(32.5%)	23(88.5%)	3(11.5%)	20(62.5%)	12(37.5%)
C1q	Positive	7(25.9%)	20(74.1%)	15(45.5%)	18(54.5%)	24(82.8%)	5(17.2%)	15(51.7%)	14(48.3%)
	Negative	3(15.8%)	16(84.2%)	16(76.2%)	5(23.8%)	10(100%)	0	12(75%)	4(25%)
lambda	Positive	10(21.7%)	36(78.3%)	31(57.4%)	23(42.6%)	34(87.2%)	5(12.8%)	27(60%)	18(40%)
	Negative	0	0	0	0	0	0	12(75%)	4(25%)
kappa	Positive	9(24.3%)	28(75.7%)	24(54.5%)	26(83.9%)	5(16.1%)	5(17.2%)	21(58.3%)	15(41.7%)
	Negative	1(12.5%)	7(87.5%)	7(70%)	3(30%)	7(100%)	0	6(75%)	2(25%)
albumin	Positive	4(33.3%)	8(66.7%)	5(38.5%)	8(61.5%)	9(81.8%)	2(18.2%)	5(41.7%)	7(58.3%)
	Negative	6(18.2%)	27(81.8%)	26(65%)	14(35%)	24(88.9%)	3(11.1%)	22(66.7%)	11(33.3%)
Fibrinogen	Positive	5(35.7%)	9(64.3%)	4(28.6%)	10(71.4%)	10(83.3%)	2(16.7%)	5(41.7%)	7(58.3%)
	Negative	5 (16.1%)	26(83.9%)	27(69.2%)	12(30.8%)	23(88.5%)	3(11.5%)	22(66.7%)	11(33.3%)

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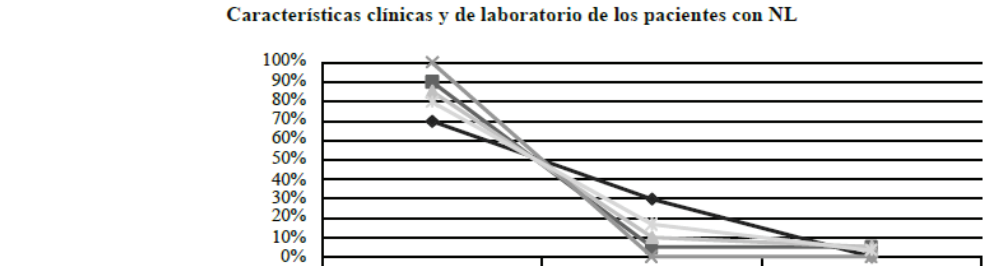
Graph 2.
Relationship of clinical and paraclinic variables with LN classes studied.



	Clase IV	Clase III	Clase II
Hipertensión	70%	30%	0%
Creatinina>=1,3 mg/dl	90%	5%	5%
Bun>=18mg/dl	85%	10%	5%
Proteinuria>=3,5gr/24h	100%	0%	0%
Hematuria	80%	16,70%	3,30%

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