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LUPUS NEPHRITIS AND RESPONSE TO TREATMENT IN LATIN AMERICA

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GLADEL LATIN AMERICA
SCIENCE & EDUCATION

BACKGROUND

- Lupus nephritis (LN) is a kidney disease caused by systemic lupus erythematosus (SLE) and affects up to 65% of patients with SLE[1]
- Current Latin American clinical practice guidelines recommend glucocorticoids and antimalarials in combination with immunosuppressants (i.e., cyclophosphamide, mycophenolate mofetil, or tacrolimus) as induction therapy and mycophenolate mofetil or azathioprine as maintenance therapy for patients with LN
- There is little information available regarding treatment response, particularly renal response, with current standard-of-care treatments in Latin American patients with LN[2]
- The Latin American Lupus Study Group (Grupo Latino Americano De Estudio del Lupus [GLADEL]) was created to explore disease features, the clinical course, and outcomes in Latin American patients with SLE[3]
  - GLADEL 2.0 is an observational prevalent and incident cohort that was initiated in 2019 in Argentina, Brazil, Chile, Colombia, the Dominican Republic, Ecuador, Mexico, Paraguay, Peru, and Uruguay[4]
- This study aimed to describe the rate of treatment response at 12 months in patients with active LN from the GLADEL 2.0 cohort

METHODS

Study population

- A total of 44 centers from 10 Latin American countries enrolled patients aged ≥18 years who fulfilled the 1982/1997 American College of Rheumatology (ACR) and/or 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria
- Patients were categorized into 4 subsets according to the presence of LN, as follows:
  - Group I: no LN
  - Group II: prevalent and inactive LN
  - Group III: prevalent and active LN
  - Group IV: incident LN with an onset of <3 months and renal biopsy
- For this analysis, patients in Groups III and IV with sufficient follow-up data at 12 months were included

Study assessments

- Baseline demographics, clinical manifestations, disease activity based on the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and SLICC/ACR Damage Index, and treatment use were assessed
- Renal response was assessed at the 12-month follow-up and was categorized according to European Alliance of Associations for Rheumatology/Kidney Disease: Improving Global Outcomes criteria, as follows:
  - Complete response (CR): <0.5 g/g reduction in proteinuria, measured as urine protein-to-creatinine ratio (UPCR) from a 24-hour urine collection
  - Partial response (PR): ≥50% reduction in proteinuria, measured as UPCR from a 24-hour urine collection
  - No response (NR): <50% reduction in proteinuria

Statistical analysis

- Continuous variables were reported as medians (interquartile ranges), and categorical variables were reported as frequencies (percentages)
- Baseline demographics, clinical characteristics, and treatment use were compared between patients in Groups III and IV using the Mann-Whitney *U* test, chi-square test, or Fisher exact test, as appropriate
- Baseline demographics, clinical characteristics, and treatment use were subsequently compared between patients with NR and PR + CR and between patients with PR and CR at the 12-month follow-up using the Mann-Whitney *U* test, chi-square test, or Fisher exact test, as appropriate

RESULTS

Patient characteristics

- A total of 1081 patients were enrolled in GLADEL 2.0; of those, 364 were eligible for and included in this analysis: 195 (53.6%) in Group III and 169 (46.4%) in Group IV
- At the 12-month follow-up, 13/364 (3.6%) patients had died, 14/364 (3.8%) had been lost to follow-up, and 28/364 (7.7%) had incomplete data; therefore, the calculation of renal response was carried out in the remaining 309 patients
- Patients in Group III had a significantly longer disease duration and significantly higher activity and chronicity indices compared to those in Group IV; Group III also had significantly higher percentages of patients with full health insurance coverage, chronic renal failure, renal histological class IV, and certain clinical manifestations (in the mucocutaneous and neuropsychiatric domains) compared to Group IV (**Table 1**)
- Patients in Group IV had significantly higher disease activity according to SLEDAI score compared to those in Group III

TABLE 1: Baseline demographics and clinical characteristics of patients with active and incident LN

	Total (N = 364)	Group III: prevalent and active LN (n = 195)	Group IV: incident LN (n = 169)	*p* value
Sociodemographic				
Age at cohort entry, y, median (IQR)	31.0 (24.8–38.9)	30.6 (25.1–38.1)	31.6 (24.1–39.6)	0.899[a]
Female, n (%)	309 (84.9)	172 (88.2)	137 (81.1)	0.058[b]
Disease duration, mo, median (IQR)	31.0 (4.0–115.5)	77.0 (27.0–139.0)	4.0 (1.0–30.0)	<0.0001[a]
Education, y, median (IQR)[c]	13.0 (11.0–16.0)	13.0 (11.0–16.0)	12.0 (11.0–16.0)	0.089[a]
Ethnic group, n (%)				0.418[b]
Caucasian	79 (21.7)	44 (22.6)	35 (20.7)	
Mestizo	254 (69.8)	137 (70.3)	117 (69.2)	
Amerindian	2 (0.5)	0	2 (1.2)	
Afro-Latin American	28 (7.7)	13 (6.7)	15 (8.9)	
Socioeconomic status, n (%)[d]				0.126[b]
High/high-middle	66 (18.3)	38 (19.7)	28 (16.8)	
Middle	142 (39.4)	83 (43.0)	59 (35.3)	
Middle-low/low	152 (42.2)	72 (37.3)	80 (47.9)	
Health insurance coverage (full), n (%)	200 (54.9)	120 (61.5)	80 (47.3)	0.011[b]
Renal manifestation, n (%)[e]				
Persistent proteinuria (>500 mg/d)	331 (91.4)	174 (89.2)	157 (94.0)	0.105[b]
Nephrotic proteinuria	152 (43.2)	78 (41.7)	74 (44.8)	0.553[b]
Acute renal failure	48 (13.4)	21 (11.0)	27 (16.2)	0.151[b]
Chronic renal failure	27 (7.5)	22 (11.5)	5 (3.0)	0.002[b]
Renal biopsy				
Activity index, median (IQR)	9.0 (5.0–25.0)	9.0 (6.0–25.0)	8.0 (5.0–14.0)	0.047[a]
Chronicity index, median (IQR)	3.0 (2.0–13.0)	4.0 (2.0–13.0)	3.0 (1.0–6.0)	0.004[a]
Renal biopsy – antiphospholipid syndrome, n (%)	8 (2.2)	4 (2.1)	4 (2.4)	0.575[b]
Renal histological class, n (%)				
Class II	22 (6.0)	10 (5.1)	12 (7.1)	0.431[b]
Class III	93 (25.5)	42 (21.5)	51 (30.2)	0.059[b]
Class IV	204 (56.0)	120 (61.5)	84 (49.7)	0.023[b]
Class V	78 (21.4)	38 (19.5)	40 (23.7)	0.332[b]
Clinical manifestations, n (%)				
Mucocutaneous domain	313 (86.0)	176 (90.3)	137 (81.1)	0.011[b]
Articular domain	296 (81.3)	162 (31.8)	134 (79.3)	0.355[b]
Serous domain	135 (37.1)	71 (36.4)	64 (37.9)	0.773[b]
Neuropsychiatric domain	36 (9.9)	25 (12.8)	11 (6.5)	0.044[b]
Hematological domain	252 (69.2)	130 (66.7)	122 (72.2)	0.254[b]
Serological domain[f]	361 (99.2)	193 (99.0)	168 (99.4)	0.647[b]
Positive lupus anticoagulant, n (%)	42 (11.5)	25 (12.8)	17 (10.1)	0.142[b]
Positive anticardiolipin, n (%)	42 (11.5)	30 (15.4)	12 (7.1)	0.066[b]
Positive anti-B2GP1, n (%)	23 (6.3)	16 (8.2)	7 (4.1)	0.286[b]
Hypocomplementemia,[g] n (%)	338 (92.9)	178 (91.3)	160 (94.7)	0.210[b]
SLEDAI score, median (IQR)	12.0 (8.0–18.0)	10.0 (6.0–16.0)	16.0 (11.0–21.0)	<0.0001[a]
SDI score, median (IQR)	0 (0–1.0)	0 (0–1.0)	0	<0.0001[a]
Comorbidities,[h] n (%)	145 (39.8)	79 (40.5)	66 (39.1)	0.776[b]

[a]Compared using Mann-Whitney *U* test. [b]Compared using chi-square or Fisher exact test. [c]Some patients had missing data. [d]1 of the following autoantibodies: ANA, anti-DNA, and anti-SM. [e]1 of the following complement markers: C3, C4, and CH50. [f]1 of the following comorbidities: hypertension, diabetes, and current smoker. ANA=Antinuclear antibody; anti-SM=Anti-Smith antibody; B2GP1=Beta-2 glycoprotein 1; DNA=Deoxyribonucleic acid; IQR=Interquartile range; LN=Lupus nephritis; mo=Month; SDI=Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLEDAI=Systemic Lupus Erythematosus Disease Activity Index; y=Year.

Treatment use

- Overall, oral glucocorticoids (prednisone or equivalent), antimalarials, intravenous (IV) cyclophosphamide, and mycophenolate mofetil were the most frequently used treatments in patients in Groups III and IV (**Table 2**)
- The use of bolus methylprednisolone was significantly higher in patients in Group IV compared to those in Group III
- The use of mycophenolate mofetil and tacrolimus was significantly higher in patients in Group III compared to those in Group IV

TABLE 2: Baseline treatment use of patients with active and incident LN

Treatment, n (%)	Total (N = 364)	Group III: prevalent and active LN (n = 195)	Group IV: incident LN (n = 169)	*p* value[a]
Prednisone or equivalent, oral	320 (87.9)	172 (88.2)	148 (87.6)	0.853
Methylprednisolone, bolus	141 (38.7)	45 (23.1)	96 (56.8)	<0.0001
Antimalarials	313 (86.0)	171 (87.7)	142 (84.0)	0.314
Azathioprine[b]	47 (13.5)	25 (12.9)	22 (14.4)	0.686
Cyclophosphamide, IV[b]	300 (86.5)	163 (84.0)	137 (89.5)	0.135
Mycophenolate mofetil[b]	285 (81.7)	171 (87.7)	114 (74.0)	0.001
Tacrolimus[b]	42 (12.1)	30 (15.5)	12 (7.8)	0.030
Cyclosporin A[b]	3 (0.9)	1 (0.5)	2 (1.3)	0.429
Belimumab[b]	8 (2.3)	6 (3.1)	2 (1.3)	0.267
Rituximab[b]	32 (9.2)	19 (9.8)	13 (8.5)	0.678

[a]Compared using Mann-Whitney *U* test. [b]Some patients had missing data. IV=Intravenous; LN=Lupus nephritis.

Renal response

- At the 12-month follow-up, 110/309 (35.6%) patients had NR, 47/309 (15.2%) had a PR, and 152/309 (49.2%) had a CR (**Table 3**)
- Patients who achieved renal response (PR or CR) had a significantly shorter disease duration, lower chronicity index, and greater use of IV cyclophosphamide compared to those with NR; furthermore, all PR and CR patients belonged to Group IV (incident LN)
  - A numerically greater use of pulse corticosteroids was also observed among patients who achieved PR or CR versus NR
- Patients who achieved CR had significantly lower baseline proteinuria and creatinine values, more frequently belonged to renal histological classes II through IV, and had a lower SLEDAI score compared to those who achieved PR

TABLE 3: Baseline demographics, clinical characteristics, and treatment use according to renal response at 12 months

	NR (n = 110)	PR + CR (n = 199)	*p* value	PR (n = 47)	CR (n = 152)	*p* value
Sociodemographic						
Age at cohort entry, y, median (IQR)	31.1 (25.2–37.8)	31.5 (25.2–40.3)	0.555[a]	28.5 (23.7–36.0)	32.1 (25.5–42.4)	0.041[a]
Female, n (%)	96 (87.3)	166 (83.4)	0.366[b]	37 (78.7)	129 (84.9)	0.322[b]
Disease duration, mo, median (IQR)	59.0 (12.0–129.0)	27.0 (4.0–104.0)	0.023[a]	23.0 (3.0–102.0)	27.5 (4.0–109.0)	0.378[a]
Education, y, median (IQR)[c]	13.0 (12.0–16.0)	12.0 (11.0–15.5)	0.184[a]	12.0 (11.0–15.0)	12.0 (11.0–16.0)	0.412[a]
Ethnic group, n (%)			0.491[c]			0.506[c]
Caucasian	23 (20.9)	48 (24.1)		9 (19.1)	39 (25.7)	
Mestizo	76 (69.1)	138 (69.3)		37 (78.7)	101 (66.4)	
Amerindian	0	1 (0.5)		0	1 (0.7)	
Afro-Latin American	11 (10.0)	11 (5.5)		1 (2.1)	10 (6.6)	
Socioeconomic status, n (%)[d]			0.578[c]			0.531[c]
High/high-middle	17 (15.5)	35 (17.9)		6 (12.8)	29 (19.6)	
Middle	40 (36.4)	78 (40.0)		19 (40.4)	59 (39.9)	
Middle-low/low	53 (48.2)	82 (42.1)		22 (46.8)	60 (40.5)	
Health insurance coverage (full), n (%)	62 (56.4)	107 (53.8)	0.717[b]	22 (46.8)	85 (55.9)	0.204[b]
LN treatment, n (%)						
Prednisone or equivalent, oral	91 (82.7)	179 (89.9)	0.067[b]	41 (87.2)	138 (90.8)	0.478[c]
Methylprednisolone, bolus	37 (33.6)	88 (44.2)	0.069[b]	22 (46.8)	66 (43.4)	0.682[b]
Antimalarials	95 (86.4)	175 (87.9)	0.689[b]	40 (85.1)	135 (88.8)	0.494[c]
Azathioprine[b]	19 (17.9)	25 (12.6)	0.210[b]	3 (6.4)	22 (14.6)	0.140[c]
Cyclophosphamide, IV[b]	94 (88.7)	189 (95.5)	0.026[c]	46 (97.9)	143 (94.7)	0.362[b]
Mycophenolate mofetil[b]	90 (84.1)	165 (83.3)	0.860[b]	40 (85.1)	125 (82.8)	0.708[b]
Tacrolimus[b]	19 (17.9)	19 (9.6)	0.036[c]	5 (10.6)	14 (9.3)	0.781[b]
Cyclosporin A[b]	1 (0.9)	2 (1.0)	0.955[c]	0	2 (1.3)	0.427[b]
Belimumab[b]	4 (3.7)	4 (2.0)	0.370[c]	3 (6.4)	1 (0.7)	0.014[c]
Rituximab[b]	15 (14.2)	14 (7.1)	0.045[c]	6 (12.8)	8 (5.3)	0.081[b]
Baseline proteinuria (g/d), median (IQR)	1.9 (0.8–4.2)	1.8 (1.2–3.8)	0.445[a]	5.4 (3.4–8.3)	1.2 (0.7–3.1)	<0.0001[a]
Baseline creatinine (mg/dL), median (IQR)	0.8 (0.7–1.2)	0.9 (0.7–1.2)	0.673[a]	1.1 (0.7–1.9)	0.8 (0.7–1.1)	0.007[a]
Renal biopsy						
Activity index, median (IQR)	10.0 (6.0–25.0)	9.0 (6.0–14.0)	0.208[a]	10.0 (7.0–14.0)	9.0 (5.5–15.0)	0.618[a]
Chronicity index, median (IQR)	5.0 (2.0–13.0)	3.0 (1.0–7.0)	0.015[a]	3.0 (2.0–6.0)	3.0 (1.0–7.0)	0.737[a]
Renal histological class, n (%)						
Class II	5 (4.5)	12 (6.0)	0.583[a]	0	12 (7.9)	0.046[a]
Class III	22 (20.0)	55 (27.6)	0.137[a]	7 (14.9)	48 (31.6)	0.025[a]
Class IV	68 (61.8)	109 (54.8)	0.230[a]	34 (72.3)	75 (49.3)	0.005[a]
Class V	21 (19.1)	43 (21.6)	0.601[a]	13 (27.7)	30 (19.7)	0.249[a]
Positive anti-DNA, n (%)	91 (82.7)	180 (90.5)	0.140[c]	45 (95.7)	135 (88.8)	0.299[c]
Hypocomplementemia,[e] n (%)	99 (90.0)	188 (94.5)	0.143[c]	45 (95.7)	143 (94.1)	0.662[c]
SLEDAI score, median (IQR)	12.0 (8.0–18.0)	12.0 (8.0–19.0)	0.237[a]	16.0 (12.0–21.0)	12.0 (8.0–18.0)	0.005[a]
Comorbidities,[f] n (%)	45 (40.9)	79 (39.7)	0.835[b]	19 (40.4)	60 (39.5)	0.907[b]
LN group, n (%)			0.0005[b]			0.850[b]
Group III: prevalent and active LN	75 (68.2)	95 (47.7)		23 (48.9)	72 (47.4)	
Group IV: incident LN	35 (31.8)	104 (52.3)		24 (51.1)	80 (52.6)	

[a]Compared using Mann-Whitney *U* test. [b]Some patients had missing data. [c]Compared using chi-square or Fisher exact test. [d]1 of the following complement markers: C3, C4, and CH50. [e]1 of the following comorbidities: hypertension, diabetes, and current smoker. CR=Complete response; DNA=Deoxyribonucleic acid; IQR=Interquartile range; IV=Intravenous; LN=Lupus nephritis; mo=Month; NR=No response; PR=Partial response; SLEDAI=Systemic Lupus Erythematosus Disease Activity Index; y=Year.

KEY TAKEAWAY

- In a cohort of patients with LN in Latin America, >80% of patients received treatments consistent with the current Latin American treatment guidelines, and two-thirds of patients demonstrated renal response at the 12-month follow-up

CONCLUSIONS

- Renal response was achieved in 64% of patients having their first episode of LN, with lower chronicity rates in the biopsy and a lower SLEDAI score in patients with PR + CR compared to those with NR
- Pulse corticosteroids, antimalarials, and IV cyclophosphamide continue to be the options chosen by most treating physicians
- More data and a longer follow-up duration will allow for the evaluation of the persistence of this response over time and the factors that may influence it

REFERENCES

1. Hocaoğlu M, et al. *Arthritis Rheumatol*. 2023;75(4):567–573.
2. Pons-Estel BA, et al. *Ann Rheum Dis*. 2018;77(11):1549–1557.
3. Pons-Estel BA, et al. *Medicine (Baltimore)*. 2004;83(1):1–17.
4. Gómez-Puerta JA, et al. *Lupus*. 2021;30(4):630–640.

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