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LUPUS AROUND THE WORLD

Childhood systemic lupus erythematosus in Latin America. The GLADEL experience in 230 children

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To evaluate disease characteristics of childhood onset SLE in Latin America and to compare this information with an adult population in the same cohort of GLADEL. A protocol was designed as a multicenter, multinational, inception cohort of lupus patients to evaluate demographic, clinical, laboratory and serological variables, as well as classification criteria, disease activity, organ damage and mortality. Descriptive statistics, chi square, Fisher´s exact test, Student´s t test and multiple logistic regression were used to compare childhood and adult onset SLE. 230 patients were < 18 years and 884 were adult SLE patients. Malar rash, fever, oral ulcers, thrombocytopenia and hemolytic anemia and some neurologic manifestations were more prevalent in children ($p < 0.05$). On the other hand, myalgias, Sjögren's syndrome and cranial nerve involvement were more frequently seen in adults ($p < 0.05$). Afro-Latin-American children had a higher prevalence of fever, thrombocytopenia and hemolytic anemia. White and mestizo children had a higher prevalence of malar rash. Mestizo children had a higher prevalence of cerebrovascular disease and cranial nerve involvement. Children met SLE ACR criteria earlier with higher mean values than adults (p: 0.001). They also had higher disease activity scores (p: 0.01), whereas adults had greater disease damage (p: 0.02). In Latin America, childhood onset SLE seems to be a more severe disease than adults. Some differences can be detected among ethnic groups. *Lupus* (2008) **17,** 596–604.

Key words: childhood; Latin America; systemic lupus erythematosus

Introduction

Systemic lupus erythematosus (SLE) is a complex, multifactorial disease of unknown aetiology in which significant immunological abnormalities have been identified. Hormonal, genetical and environmental factors have been implicated in its aetiology.[1] Its incidence is higher in women of childbearing age, but it may develop at any age, and approximately 15% of cases appear in children and teenagers.[2] Several studies have evaluated its epidemiological, clinical and serological characteristics.[3–8] Disease severity according to the age at presentation has been studied with contrasting results.[9–11] Some studies have directly compared adult and paediatric SLE populations in terms of clinical presentation, serology, immunogenetics and prognosis.[12–15] The discrepancies found are likely due to differences in inclusion criteria, i.e. age at baseline, different end-point definitions and genetic variables, making it difficult to compare all the existing published data.

The study of SLE in children offers some advantages such as the lower prevalence of several comorbid factors, e.g. abnormal lipid metabolism, alcohol intake and smoking.[16] The GLADEL (Grupo Latino Americano de Estudio del Lupus) cohort,[17] with a total of 1214 patients, offers excellent possibilities for evaluating disease characteristics of childhood SLE in Latin America and for comparing this information with the adult population evaluated within the same cohort, using standardized information gathered systematically. The objectives of this study were to describe the clinical characteristics of a population with childhood SLE, and to explore differences and similarities with an adult population having the same

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disease seen in Latin-American rheumatology centers, using the same clinical protocol.

Patients and methods

Study design

Information for this study was obtained from a prospective inception cohort from GLADEL, consisting of 34 centers distributed throughout nine Latin-American countries, and using a computerized database that included the following end-points: demographic, clinical manifestations, laboratory findings, treatment, disease activity indexes such as SLEDAI [18] and MEXSLEDAI,[19] the SLICC damage index (SDI),[20] complications and mortality.

Patients

Patients were included if they had received a diagnosis of SLE by a qualified internist or rheumatologist. Fulfilment of four classification criteria of the American College of Rheumatology (ACR)[21,22] at the time of diagnosis was not mandatory. Each center incorporated 20–30 patients at baseline and then added one new randomized patient each month during a period of 2 years. These number of patients were initially selected to maintain a balanced representation between centers. All patients were interviewed by a rheumatologist or a qualified internist with experience in SLE and the randomization was locally done at each center. The first patients joined the study in October 1997 and to insure their recent onset, they could only be included if their diagnosis of SLE had been made since 1 January 1996. It was also necessary that the diagnosis must be registered in the clinical chart according to the ACR or other widely accepted criteria.[23] Most of these centers treat children and adult patients with SLE. Thirty-two out of the 34 centers included children with SLE in the following numbers: Mexico 55, Brazil 46, Argentina 45, Colombia 32, Venezuela 21, Chile 17, Peru 7, Cuba 4 and Guatemala 3 for a total of 230 children. Missing data were detected in 11.3% of children and 14.8% of adults. These missing values were not taken into account in the analysis. The total group of patients was divided into two subgroups, according to the age at symptoms onset, with patients under 18 years of age in the paediatric lupus group and those 18 years of age or older in the adult lupus group. All patients in this cohort were clinically evaluated according to the usual rheumatology practice at each center. For protocol purposes, it was necessary to update the clinical information for all subjects at least every 6 months for most clinical variables including disease activity indices and every year for SDI.

Laboratory testing was performed in all participating centers in their local laboratories with standardized techniques. Auto-antibodies and complement testing were also performed at all the centers with their respective cut-off values considered as valid.

Variable definitions

Ethnic groups

An operational definition was necessary. It was developed by consensus, with an expert in immunogenetics participating. These definitions were determined according to the parents' and all four grandparents' self-reported ethnicity. Patients were asked about their place of birth, as well as that of their parents and grandparents. They were thus classified as the following: White, individuals with all white European ancestors; Mestizo, individuals born in Latin America who had both Amerindian and White ancestors; African-Latin Americans (ALA): individuals born in Latin America with at least one African ancestor, irrespective of whether other ancestors were White or Amerindian. Pure Amerindians were those individuals who had all autochthonous ancestors. Final assignment of patients was the prerogative of the clinician, who also considered anthropomorphic characteristics in each case.

Socioeconomic status

This was evaluated using the Graffar method, a validated scale previously used in Latin America. The Graffar scale takes into account five variables: parents' occupation, parents' level of education, main source of income, housing and neighbourhood quality. Each variable has five categories with independent and progressive scores. A final score classifies subjects into five categories: high, medium-high, medium, medium-low and low.

Type of medical care was divided into the following categories: institutional, patients primarily treated in public institutions; partial coverage, patients who receive limited support toward medical care expenses; complete coverage, patients who have all expenses paid for; without coverage, patients who have no economic support and have to pay for all their medical expenses; private, patients cared for in private practice or institutions; with coverage, patients with prepaid or insurance-paid support; without coverage, patients who pay for their private care; education,: considered 0 (illiterate) and up to 20 years of formal education[17]; database, at baseline, ARTHROS 2.0[24] was used in all the centers. Later, ARTHROS 6.0, which is a user-

friendly database designed by Argentine rheumatologists, was used.

All researchers were similarly trained for the use of the database, and data were collected by clinicians with experience in its use. Strict data control in a single center was undertaken. All researchers followed local regulations according to their institutional review boards.

Definitions of proteinuria, thrombocytopenia, leucopenia and lymphopenia were those provided by the ACR.[22] Haemolytic anaemia was defined as a decrease in haemoglobin levels >3 g/dl and reticulocyte count >5% and a positive Coombs test. Sicca was defined with xerophthalmia through a positive Schirmer's test and xerostomia with the clinical description of dry mouth. Fever was defined as a temperature >38 °C.

Statistical analysis

SPSS 11.5 (SPSS Inc., Chicago IL, USA) software was used to analyse the data. In the univariate analysis, we used proportions and percentages for demographic, clinical and serological variables; and medians for quantitative variables with the respective interquartile range. In the bivariate analysis of qualitative variables, the measures for strength of association were obtained using the odds ratio and 95% confidence intervals, with the chi-squared test or Fisher's exact test. The Student's *t*-test was applied for quantitative variables following a normal distribution, and otherwise Mann–Whitney *U*-test was used. No adjustment for multiple comparisons was made.

In order to determine the relative weight of different dependent variables (renal impairment, lymphopenia, disease activity and death), a multivariate exploratory model using logistic regression was performed. All models were adjusted for variables that researchers anticipated might distort the relationship between child/adult and the dependent variables (such as gender, level of formal education, socioeconomic status and health coverage). A p-value <0.05 was considered as statistically significant.

Results

General characteristics

A total of 1214 patients were registered in the GLADEL database, from 34 centers and nine countries. Of these, 230 (18.9%) were children, with 207 (90%) females and 23 (10%) males, at a 9:1 ratio; and 984 (81.1%) were adults, with 884 (89.8%) females and 100 (10.2%) males, at an 8.8:1 ratio. We included 18 (7.8%) patients between 0 and 9 years old and 212 (92.2%) patients between 10 and 18 years old. Ethnic distribution by group was as follows: children, 102 (44.4%) were Mestizo, 93 (40.4%) White and 35 (15.2%) ALA; and adults, 435 (44.2%) were Mestizo, 414 (42.1%) White, 117 (11.9%) ALA and 18 (1.8%) other ethnic groups. There were no statistical differences in ethnic distribution and age at presentation. Mean age at symptoms onset was 15.3 (13.2–16.7) years and 29.1 (23.2–37.5) years for children and adults respectively (see Table 1). Time taken for diagnosis was less in children than adults: 0.35 (0.16–1.62) years vs. 0.51 (0.22–1.34) years, $p = 0.74$, and follow-up was similar in both groups. We evaluated the median time for meeting four SLE criteria, and children had a median time of 2.04 months, whereas adults had a median time of 4.4 months ($p < 0.001$). At baseline, 13 children (5.7%) and 52 adults (5.3%) did not fulfil ACR classification criteria. The most common criteria in this subgroup of patients were: positive antinuclear antibodies (80%), haematological criteria (56.9%) and arthritis (46.2%).

Table 1 General characteristics

Characteristics	*Children (IQR)*	*Adults (IQR)*	p-*value*
Male: female ratio	9:1	8.8:1	
Years of education	9 (7.0–11.0)	10 (7.0–13.0)	
Age of symptoms onset (years)	15.3 (13.2–16.7)	29.1 (23.2–37.5)	
Age at diagnosis (years)	16.4 (14.2–17.8)	30.8 (24.3–39)	
Time to diagnosis (years)	0.35 (0.1–1.6)	0.5 (0.2–1.3)	0.06
Number of hospitalizations	1.0 (0–1.0)	1.0 (0–1.0)	0.8
Days of hospitalization	5.0 (0–21)	4.0 (0–21)	0.6
Years of follow-up	1.7 (0.8–2.9)	1.6 (0.8–2.7)	0.7
Duration of the disease (years)	2.6 (1.4–4)	2.6 (1.5–3.9)	0.6

Abbreviation: IQR: interquartile range.

Clinical findings

Upon comparing the clinical findings in both study groups, we found statistically significant difference between them. Malar rash (70.4%), fever (63.5%), oral ulcers (49.1%), thrombocytopenia (25.2%) and haemolytic anaemia (16.1%) were more frequently seen in children (Table 2). The predominant findings in the adult population were myalgias (18.9%), sicca syndrome (9.3%) and cranial nerve involvement (4.2%).

Eye involvement was the only systemic involvement more frequently seen in adults ($p = 0.006$). Table 3 shows differences in classification criteria between the two age groups of SLE patients.

When we evaluated the number of classification criteria, disease activity and disease damage between the adult and paediatric groups, we only found statistically

Table 2 Main clinical and laboratory differences in children and adults with SLE

	Children		*Adults*			
Characteristic	N = *230*	*%*	N = *984*	*%*	p-*value*	*OR (95% CI)*
Fever	146	63.5	543	55.2	0.02	1.4 (1–1.8)
Myalgias	27	11.7	186	18.9	0.01	0.57 (0.3–0.8)
Xerophthalmia	4	1.7	65	6.6	0.004	0.25 (0.09–0.6)
Sicca syndrome	9	3.9	92	9.3	0.007	0.3 (0.2–0.7)
Oral ulcers	113	49.1	393	39.9	0.01	1.4 (1.09–1.9)
Chorea*	5	2.2	0	0.0	0.000	
Pseudotumor cerebri*	2	0.9	0	0.0	0.03	
TIA*	2	0.9	0	0.0	0.03	
CVA	12	5.2	22	2.2	0.01	2.4 (1.1–4.9)
Cranial nerve lesion	3	1.3	41	4.2	0.03	0.3 (0.09–0.9)
Haemolytic anaemia	37	16.1	106	10.8	0.02	1.5 (1.06–2.3)
Malar rash	162	70.4	582	59.1	0.002	1.6 (1.2–2.2)
Creatinine >1.5 mg/dl	29	12.6	182	18.5	0.03	0.6 (0.4–0.9)
Thrombocytopenia	58	25.2	175	17.8	0.01	1.5 (1.1–2.1)
IgM aCL	47	20.4	130	13.2	0.05	1.5 (0.9–2.4)

*Fisher's exact test.
Abbreviations: TIA: transient cerebral transitory ischaemia; CVA: cerebrovascular accident; aCL: anticardiolipin.

Table 3 Prevalence of Classification Criteria of the American College of Rheumatology in children and adults with SLE

	Children		*Adults*		
Criteria	N = *230*	*%*	N = *984*	*%*	p-*value*
Arthritis	191	83.0	807	82.0	0.7
Photosensitivity	122	53.0	559	56.8	0.3
Malar rash*	162	70.4	582	59.1	0.002
Discoid rash	29	12.6	114	11.6	0.6
Oral ulcers†	113	49.1	393	39.9	0.01
Pleuritis	40	17.4	228	23.2	0.5
Pericarditis	39	17.0	170	17.3	0.9
Proteinuria/cellular casts	113	49.1	446	45.3	0.2
Psychosis	11	4.8	38	3.9	0.5
Seizures	26	11.3	73	7.4	0.05
Haemolytic anaemia‡	37	16.1	106	10.8	0.02
Leucopenia	106	46.1	408	41.5	0.2
Lymphopenia	139	60.4	581	59.0	0.6
Thrombocytopenia§	58	25.2	175	17.8	0.01
Positive ANA	216	96.9	921	98.2	0.3
Anti-DNA	124	67.0	540	71.3	0.2
Anti-Sm	58	51.3	209	47.6	0.5
False-positive VDRL	18	31.0	71	28.7	0.8
IgG aCL	57	51.8	205	50.2	0.8
IgM aCL	47	47.5	130	36.8	0.05
Lupus anticoagulant	11	34.4	48	29.6	0.7

Abbreviations: ANA: antinuclear antibodies; aCL: anticardiolipin.
*OR 1.65 (95% CI 1.21–2.24); †OR 1.45 (95% CI 1.09–1.94); ‡OR 1.59 (95% CI 1.06–2.39); §OR 1.56 (95% CI 1.11–2.19); ¶OR 1.55 (95% CI 0.99–2.43).

significant differences favouring the paediatric group in the number of classification criteria, in the maximum SLEDAI, and the maximum MEXSLEDAI, and favouring adults in the maximum SDI (see Table 4).

Ethnic groups

Ethnicity and age group were also evaluated. Differential results were reported according to the ethnic group, and they were significantly different in the ALA population for haematological symptoms and fever; in the Mestizo and White populations for cutaneous symptoms and in the Mestizo population for central nervous system involvement. However, when we evaluated ethnic groups adjusted by age with all variables having statistically significant difference, we found that White patients were more likely to present fever (OR 1.6, 95% CI 1–2.7); malar rash (OR 1.84, 95% CI 1.1–3) and less likely to present myalgia

Table 4 Disease activity and damage indexes in children and adults with SLE

Characteristic	*Children (IQR)*	*Adults (IQR)*	p-*value**
Cumulative diagnostic criteria	5.9 (5–7)	5.7 (5–7)	0.009
SLEDAI	2 (1–4)	2 (1–3)	0.2
Maximum SLEDAI	13 (8–19)	11 (7–17)	0.01
Mean SLEDAI	7.3 (4–13.9)	7 (4–11)	0.07
MEXSLEDAI	3 (1–4)	2 (1–3)	0.5
Maximum MEXSLEDAI	8 (5–11)	7 (4–11)	0.05
Mean MEXSLEDAI	5 (2.5–9)	4.3 (2.3–7.3)	0.09
SDI	2 (1–3)	2 (1–3)	0.3
Maximum SDI	0.0 (0.0–1)	0.0 (0.0–1)	0.02
Mean SDI	0.0 (0.0–0.3)	0.0 (0.0–0.5)	0.02

Abbreviation: IQR: interquartile range.
*Mann–Whitney *U*-test.

(OR 0.4, 95% CI 0.2–0.9). Afro-Latin American lupus patients had a higher risk to develop fever (OR 3.1, 95% CI 1.2–7.7), haemolytic anaemia (OR 3.7, 95% CI 1.2–11.1), thrombocytopenia (OR 3, 95% CI 1.2–7.5) and IgM aCL antibodies (OR 4.5, 95% CI 1.6–12.6).

Mestizos had a higher risk to present ischaemic cerebrovascular accident (OR 3.3, 95% CI 1.1–9.8) and malar rash (OR 1.9, 95% CI 1.2–3.1), and less likely to develop myalgia (OR 0.52, 95% CI 0.2–1), sicca syndrome (OR 0.2, 95% CI 0.08–0.9) and serum creatinine levels >1.5 mg/dl (OR 0.5, 95% CI 0.2–1).

Multivariate analysis

In the multivariate model, we found that belonging to one age group or the other is not a major predictive factor for renal impairment, lymphopenia or death; however, it does seem to be a major predictive factor for decreased activity in the adult population when compared with children, with SLEDAI (OR 0.5, 95% CI 0.4–0.7, $p = 0.001$) and MEXSLEDAI (OR 0.6, 95% CI 0.4–0.8, $p = 0.003$) respectively (Table 5).

Regarding family history of autoimmunity, we found that the paediatric population was more likely to have a higher prevalence of autoimmune diseases in second degree consanguinity [grandparents, grandsons, uncles, nephews and cousins] (6.9% vs. 1.8%) (OR 3.7, 95% CI 1.9–7.3, $p < 0.001$).

Laboratory findings

Although, immunological tests were not systematically performed in a single reference center, but rather in local laboratories of participating centers, we might point out that the only test between the two populations that demonstrated a trend was IgM aCL antibodies, which indicated higher frequency in children, as previously mentioned in Table 2.

Other outcomes

There were 662 hospitalizations, and no differences were found between children and adult patients in the frequency and type of hospitalization. Finally, 34 patients died during the study, including nine in the paediatric group (3.8%) and twenty-five in the adult group (2.5%), with no statistically significant difference. Causes of death in both groups were by disease activity (five children, seven adults); infection (four adults) or both disease activity and infection (three children, 13 adults); cancer (one adult) and unknown (one child). The most significant organ involvement due to disease activity was: renal (16 patients), multiorgan (4), central nervous system (4), lung (3) and haematological (1). The infections involved were: septicaemia (10), pneumonia (6), peritonitis (3) and meningitis (1). The isolated organisms were: *Staphylococcus aureus*, *Candida* sp., *Mycobacterium tuberculosis*, *Pneumocystis carinii*, *Pseudomonas* sp. and *Enterococcus faecalis*.

Discussion

On the basis of the GLADEL cohort, which is a prospective, multicentre and multinational cohort in Latin-American countries, we analysed the differences in SLE between adults and children. Latin America has a vast conglomerate population with significant

Table 5 Multivariate model to analyse belonging to an age group as a major effect in adults and children with SLE in GLADEL cohort

		Renal impairment model	*Lymphopenia model*	*SLEDAI model ≥12 vs. <12*	*MEXSLEDAI model ≥8 vs. <8*	*Death model*
Age group		*Yes vs. no (n = 428/n = 586)*	*Yes vs. no (n = 720/n = 494)*	*Yes vs. no (n = 365/n = 849)*	*Yes vs. no (n = 355/n = 859)*	*Yes vs. no (n = 34/n = 1180)*
Children	OR	1.0	1.0	1.0	1.0	1.0
Adults	OR	0.92	0.97	0.57	0.61	0.70
	95% CI	0.68–1.25	0.72–1.56	0.72–1.56	0.41–0.79	0.31–1.61
	p	0.598	0.793	0.001	0.003	0.401

interbreeding within each country and between countries, and consequently, clinical studies conducted in this heterogeneous context are especially valuable. It is important to emphasize that this paper presents unique information regarding SLE in childhood, particularly infrequent in published literature from Latin America.

Paediatric SLE accounts for about 15% of all patients with this disease, however, findings vary in different studies due to the age limit used to define the paediatric group. In our study, and in line with other authors,[8,12,25,26] we established the age limit as <18 years at the beginning of the symptoms and we found a frequency of 18.9% that is similar to the age range described in other papers.[12–14,26] Proportions by gender were similar in both groups, and this might be explained by the low SLE frequency during the first decade of life in this study (18 children, 7.8%) and reported by some researchers,[14,27] but in contradiction with other papers on paediatric SLE.[12,25,26] The median age for children SLE was 15.3 years, and for adults, 29.1 years, and time taken for diagnosis was less in the paediatric group, although without significant differences with adult-onset SLE (median of 129.5 days vs. 186.5 days, $p = 0.065$). This differs from that reported by European authors, in which case the time taken for diagnosis is greater in paediatric SLE.[13,14] This particular difference could be due to increased disease severity in childhood SLE in Latin America, which is supported by fever, higher SLEDAI scores and faster ACR classification criteria fulfilment in our study.

Regarding the different clinical and laboratory manifestations, the data in the literature varies with regard to the type of predominant involvement in one age group or the other. Meislin, *et al.*[11] defined that the only difference was the presence of hepatosplenomegalia and/or lymphadenopathy found twice as often in children. Font, *et al.*[14] described more significant renal involvement, malar rash, fever and chorea in children, whereas for Tucker, *et al.*[12] the most frequent involvement in children is haematological, and in adults cardiopulmonar. Meanwhile, other authors[6,25] found haematological involvement to be less frequent in children. In Eurolupus, the differential findings with children were malar rash and nephropathy.[13] Recently, the only statistically significant difference in a Spanish study was the presence of arthritis in children.[26] In our observations, some of the most frequent findings in children were: malar rash, fever, oral ulcers, thrombocytopenia, haemolytic anaemia and IgM aCL antibodies.

Our study indicates a higher frequency of haematological abnormalities, such as thrombocytopenia, haemolytic anaemia and positive IgM antiphospholipid antibodies, as also described in the literature,[28–32] and we found that when the OR is adjusted, it is maintained as a significant association in ALA children, but not in Whites and Mestizos, which undoubtedly reflects the heterogeneity of the Latin-American population. Moreover, we must emphasize central nervous system involvement, despite its low frequency, expressed as chorea, transient ischaemic attacks and cerebrovascular accidents, which occur more often in the paediatric population. In this case, our findings differ from other reports,[28,29,33] and suggest a greater severity of SLE in this age group, likely explained in part by the association with antiphospholipid antibodies.[28,29,34–36]

In the univariate analysis, we found a significantly higher frequency of creatinine above 1.5 mg/dl in the adult group, although the multivariate analysis of renal impairment did not establish any differences, and this differs from other studies that mention a more frequent renal impairment in children.[13,14,25,26] This can likely be explained by our cut-off point for an abnormal creatinine value >1.5 mg/dl, and this value could underestimate the diagnosis of renal insufficiency in the paediatric age group.

When we analysed classification criteria, the mucocutaneous and haematological involvement in the paediatric population was more prevalent than in other series,[8,37,38] and the number of the cumulated classification criteria was only slightly higher in children, although statistically significant ($p = 0.009$). When evaluating the maximum achieved disease activity score in both age groups, both the SLEDAI and MEXSLEDAI were higher in children, and this tendency persisted in the multiple logistic regression model. The situation was different for the SDI, which was higher in adults, although not statistically different. In this case we coincide with Miettunen, *et al.*,[39] who did not find any influence from age, gender or race; and we differ from another Canadian study in which the children cumulated damage more quickly than adults after an average of 3.3 years of disease duration.[40]

Mortality in SLE is characterized by a bimodal manner,[41,42] with early death due to disease activity and a late mortality associated with cardiovascular events. With a median follow-up of 20 months, 34 deaths occurred in this trial, with nine in the paediatric group (3.8%) and 25 in the adult population (2.5%), without a statistically significant difference.

As reported by other authors[5,8,43–45] in studies in which early death occurs, the causes of death in this study during the first 5 years of follow-up were disease

activity and infection, plus other non-SLE-related causes such as cancer and unknown causes.

The organ involved responsible for death in those presenting disease activity was renal (47.1%), multisystemic (14.7%), central nervous system (11.8%), pulmonary haemorrhage (8.8%), septicaemia (29.4%), pneumonia (17.6%) and peritonitis (8.8%). Infection was a common mortality cause coinciding with other groups.[8,16,42,45]

One of the strengths of this research is that it evaluates a disease, such as SLE, in a highly heterogeneous population, such as that of Latin America, with a significant number of patients, especially in the paediatric group, plus it uses a prospective inception cohort. However, we have to recognize some limitations in our study, such as a relatively short follow-up period, laboratory data was not evaluated at a single reference center and some laboratory tests, such as antiphospholipid antibodies, depend on the experience and techniques used in different laboratories, and probably the local randomization process.

The findings in our population allow us to conclude that paediatric lupus has a more severe presentation due to higher disease activity indexes, with major haematological, cutaneous and central nervous system involvement. We found that the most affected groups in the GLADEL cohort are the ALA and Mestizo populations.

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With the corresponding attributes and responsibilities.