LUPUS SCIENCE & MEDICINE™

Frequency and associated factors of herpes zoster infection in SLE patients from Latin America: data from the GLADEL 2.0 cohort

Romina Nieto ,[1,2] Lucia Hernández,[3] Marina Scolnik,[4] Laura Maurelli,[5] Carla Gobbi,[6,7] Veronica Saurit,[8] Lucila Garcia,[9] Boris Kisluk,[10] María Constanza Bertolaccini,[11] Melissa Serna Góngora,[12] Graciela N Gómez,[13] Cecilia Pisoni,[14] Ana Carolina Ralle,[15] Paola Pirruccio,[16] Vitalina de Souza Barbosa,[17] Andrese Gasparin,[18] Angela Duarte,[19] Laíssa Cristina Alves Alvino,[20,21] Eduardo F Borba ,[22] Eloisa Bonfá,[23] Edgard Torres dos Reis-Neto ,[24] Alexis Bondi Peralta,[25] Loreto Massardo,[26] Gustavo Aroca Martínez,[27,28] Antonio Iglesias Gamarra,[27,28] Carlos A Cañas,[29] Gerardo Quintana López,[30] Leon Frederick Silvery,[31,32] Jose Maximiliano Martinez ,[33] Reyna Sánchez-Briones,[34,35] Mario Pérez Cristóbal,[36] Eduardo Martín-Nares ,[37] Luis H Silveira,[38] Ignacio García De La Torre,[39] Julio César Ramírez Sánchez,[40] Jorge Antonio Esquivel-Valerio,[41] Jhonatan Losanto,[42] Marcos Aurelio Vazquez,[42] Magaly Alva Linares,[43] Manuel F Ugarte-Gil,[44,45] Armando Calvo-Quiroz,[46] Teresandris Polanco,[47] Carina Pizzarossa,[48] Gonzalo Silveira,[49] Bernardo A Pons-Estel ,[1] Graciela S Alarcon,[50] Guillermo Pons-Estel[1]

To cite: Nieto R, Hernández L, Scolnik M, *et al*. Frequency and associated factors of herpes zoster infection in SLE patients from Latin America: data from the GLADEL 2.0 cohort. *Lupus Science & Medicine* 2026;**13**:e001877. doi:10.1136/lupus-2025-001877

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/lupus-2025-001877).

Received 20 November 2025
Accepted 18 February 2026

For numbered affiliations see end of article.

Correspondence to
Dr Guillermo Pons-Estel; gponsestel@yahoo.com

ABSTRACT

Objective The aim of this study was to assess the epidemiological and clinical characteristics of herpes zoster (HZ) and to identify the factors associated with its first episode in Latin American SLE patients.

Methods GLADEL 2.0 (Grupo Latino Americano De Estudio del Lupus) is a multiethnic, Latin American observational cohort of SLE patients. Demographic, clinical, laboratory, treatment and disease activity/damage data were compared between patients with and without HZ; its prevalence was assessed at cohort entry, incidence rates of first and recurrent HZ infections were calculated based on person-years of follow-up. Logistic regression was used to identify factors associated with HZ events, while Cox regression was used to determine the variables associated with time to first event.

Results Among 1083 SLE patients, the HZ cumulative incidence after its diagnosis was 11.5%, with a prevalence of 8.6% at cohort entry. During 5-year of follow-up, the incidence of HZ was 2.9% and 16.8% patients had recurrent episodes. Patients with HZ showed higher frequencies of alopecia, psychosis and seizures, along with higher disease activity, damage accrual, proteinuria and higher daily prednisone doses prior to the event. Multivariate analyses identified female sex, higher SLE Disease Activity Index 2000 (SLEDAI-2K) and higher daily prednisone dose as independent predictors of HZ occurrence. Older age at diagnosis, psychosis, disease activity and a higher daily prednisone dose were associated with a shorter time to HZ onset.

Conclusion In the GLADEL 2.0 cohort, the high burden of HZ in SLE, together with its association with active disease, corticosteroid exposure and neuropsychiatric manifestations, underscores the need for proactive risk stratification in clinical practice.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with SLE have a higher risk of developing herpes zoster (HZ) than the general population.
⇒ Disease activity, lymphopenia and the use of immunosuppressive drugs have been identified as potential risk factors.
⇒ Data on HZ epidemiology and risk factors among Latin American patients with SLE are scarce.

INTRODUCTION

SLE is an autoimmune disease with complex multiorgan system involvement and diverse clinical manifestations. Its incidence is estimated between 1 and 10/100 000 person-years, and its prevalence between 20 and 70/100 000.[1] Herpes zoster (HZ) is caused by the reactivation of latent varicella zoster virus (VZV) in patients who were exposed to it, often decades earlier. The infection typically manifests as an acute, painful vesicular rash that presents in a dermatomal distribution

WHAT THIS STUDY ADDS

⇒ This study provides real-world evidence on the incidence and clinical characteristics of HZ in patients with SLE from a large Latin American cohort.
⇒ Disease activity and corticosteroid dose were identified as the main predictors of HZ occurrence in Latin American patients.
⇒ Most HZ episodes were localised and had a favourable outcome, with postherpetic neuralgia and hospitalisation as the main complications.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings underscore the need for preventive strategies, including vaccination, particularly in patients with active disease or receiving high-dose corticosteroids.
⇒ The study supports the inclusion of HZ risk assessment into the routine management of patients with SLE.

and may be followed by persistent post-HZ pain (postherpetic neuralgia (PHN)).[2] There is a higher prevalence and incidence of HZ in immunocompromised patients compared with the general population, and its incidence is approximately sixfold higher in SLE patients.[3] Recurrent infection is most commonly seen in elderly and immunocompromised subjects, including those with malignancies, acquired immune deficiency syndrome and autoimmune diseases such as rheumatoid arthritis (RA) and SLE.[4 5]

A meta-analysis evaluating factors associated with an increased risk of HZ infection in the general population revealed that, among the autoimmune diseases, RA (pooled RR, 1.67; 95% CI 1.41 to 1.98) and SLE (pooled RR, 2.10; 95% CI 1.40 to 3.15) were associated with higher risk.[6] In another meta-analysis, a range of risk factors associated with HZ were identified; patients with immunosuppressive diseases, such as transplant recipients (OR=4.51), SLE (OR 2.87) and cancer (OR=2.42), were at increased risk. Notably, the risk associated with SLE exceeded that observed for cancer.[7] Certain risk factors in SLE patients have been identified in the literature, including lymphopenia,[3] disease activity, disease damage and immunosuppressive therapies.[8] In the Toronto Lupus Clinic cohort,[4] HZ prevalence was 30.5% and its incidence was 14.3 cases per 1000 person-years. Lymphopenia and higher glucocorticoid (GC) doses were significantly associated with HZ events. Likewise, in a case–control study from Taiwan, lymphopenia, anti-Ro/anti-RNP autoantibodies, renal involvement and cyclophosphamide (CYC) use were associated with an increased risk of HZ in SLE patients.[9] In a Brazilian cohort, HZ was diagnosed in 51 SLE patients (4.5%) with an annual incidence rate of 6.4 events/1000 patient-years, 19.6% had PHN and high percentages of corticosteroids and immunosuppressants use were observed among patients with HZ.[10]

The epidemiology of HZ infection has been described mainly in high-income countries where longer life expectancy is common. In contrast, data from low-income and middle-income countries, including those in Latin America, are limited.

The aim of this study was, therefore, to describe the epidemiological, sociodemographic and clinical characteristics of HZ infection in SLE, to identify the factors associated with its first episode, to assess the HZ infection recurrence rate and to explore underlying predisposing factors in Latin American SLE patients using data from the GLADEL 2.0 (Grupo Latino Americano De Estudio del Lupus) cohort.

METHODS

GLADEL 2.0 is an observational, multinational and multiethnic cohort, started in 2019.[11] The 43 centres participating in this cohort are distributed across 10 Latin American countries (Argentina, Brazil, Chile, Colombia, Dominican Republic, Ecuador, Mexico, Paraguay, Peru and Uruguay). SLE patients according to the 1982/1997 American College of Rheumatology (ACR)[12] and/or the 2012 Systemic Lupus International Collaborating Clinics (SLICC),[13] age≥18 years. Cumulative clinical and laboratory data were collected at the baseline visit using ARTHROS Web; follow-up visits occurred at 6 months and then annually. Longitudinal analysis for the occurrence of HZ infections included data collected between May 2019 and February 2025. The characteristics of HZ infection, such as the presence of ocular involvement, meningitis, disseminated infection, PHN, treatments and factors associated with its occurrence, were assessed. Data on HZ infections before cohort entry and during follow-up were self-reported by patients and confirmed by GLADEL investigators.

Patient and public involvement

Patients or the public were not involved in the design, conduct, data analysis, reporting or dissemination of this study.

Statistical analysis

The incidence rates of the first HZ infection and of its recurrence were calculated as the ratio of the overall number of HZ episodes over the cumulative person-years of follow-up (total time from the first clinic visit (T0) to the date of the last visit for all patients) from patient enrolment into the GLADEL 2.0 cohort through February 2025. The prevalence at the baseline visit was calculated as the proportion of patients with HZ infection among the 1083 in this cohort. Demographic, clinical, disease activity (SLE Disease Activity Index 2000, SLEDAI-2K),[14] damage (SLICC/ACR Damage Index),[15] laboratory, treatment and hospitalisations data of patients were compared according to the presence or absence of HZ events. The clinical presentation patterns of HZ infection are summarised using descriptive statistics. Continuous variables are presented as means±SD or medians (IQR) and categorical variables as counts (percentages). Demographic and clinical characteristics of patients with and without HZ were compared using Student's t-test, Wilcoxon, Pearson's χ^2 or Fisher's exact tests for continuous and categorical variables, as appropriate.

All HZ events included in the analysis occurred after the diagnosis of SLE. For prevalent HZ cases at cohort entry, associated factors were assessed using cumulative data collected at the baseline visit. For incident HZ events occurring during follow-up, clinical characteristics (history of prior manifestations), disease activity and medication exposure were evaluated using data from the visit immediately preceding the HZ event. Clinically significant factors were identified, and logistic regression was used to evaluate their adjusted effects on the risk of experiencing at least one episode of HZ infection from diagnosis to the end of follow-up. The results are presented as ORs and their 95% CIs. A descriptive analysis was performed to determine the characteristics of HZ events that required hospitalisation. Cox regression analysis was performed from the diagnostic date to the date of the first HZ event, or to the most recent visit in which the patient remained HZ free. All variables that had exhibited a p value≤0.10 in the univariate models were included in the multivariate analysis. All analyses were performed with the R V.4.2.2 (or a later version).[16] P values<0.05 were considered statistically significant.

RESULTS

Of the 1083 patients included in the GLADEL 2.0 cohort, an overall incidence of HZ infection after SLE diagnosis (125 cases, 11.54%) was recorded (95% CI 9.73 to 13.63). A history of HZ infection was recorded in 93 cases at the baseline visit, with a prevalence of 8.6% (95% CI 7.02 to 10.46) at cohort entry. After 5-year follow-up, 32 new cases of HZ were recorded in the entire population, representing an incidence of 2.9% (95% CI 2.06 to 4.19), and an incidence rate per 100 person-years of 3.49 (95% CI 2.92 to 4.16), with a total follow-up time of 3578.6 patients-years. Recurrent HZ infection occurred in 21 patients (16.8%, 95% CI 10.93 to 24.77), with a recurrence rate of 0.59 (95% CI 0.36 to 0.89) per 100 person-years.

Sociodemographic data

Table 1 describes the sociodemographic characteristics of patients with and without HZ infection. Most patients were female (89.6%) with a median (IQR) age at diagnosis of 27.0 years (20.6–35.4). There were no significant differences in terms of sex, age at diagnosis, ethnicity, education level and socioeconomic status between patients with or without HZ infection.

Clinical characteristics of SLE patients with HZ

Table 2 depicts the clinical manifestations of patients at admission into the cohort according to the history of HZ infection. Significantly higher frequencies of alopecia (74.4 vs 64.1, p=0.028), psychosis (7.2 vs 2.9, p=0.030) and seizures (10.4 vs 4.4, p=0.008) were observed in patients with HZ infection vs those without it. Neuropsychiatric (NP) involvement, including psychosis and seizures, was defined as a history of physician-confirmed NP lupus at any time prior to HZ event. In addition, patients with HZ infection were found to have higher cumulative damage

Table 1 Baseline characteristics in SLE patients with and without herpes zoster (HZ) events

Variable	Total (n=1083)	HZ infection (n=125)	No HZ infection (n=958)	P value*
Female, n (%)	970 (89.6)	116 (92.8)	854 (89.1)	0.275
Age at diagnosis (years), median (Q1–Q3)	27.0 (20.6–35.4)	26.1 (19.7–34.8)	27.1 (20.7–35.9)	0.245
Education level (years), median (Q1–Q3)	13.0 (11.0–16.0)	13.0 (10.5–16.0)	13.0 (11.0–16.0)	0.667
Ethnicity, n(%)				0.062
Mestizo	701 (65.0)	71 (56.8)	630 (66.0)	
White	277 (25.7)	41 (32.8)	236 (24.7)	
African Latin American	90 (8.3)	10 (8.0)	80 (8.4)	
Other	11 (1.0)	3 (2.4)	8 (0.8)	
Socioeconomic status, n(%)				0.663
Low/middle low	438 (41.0)	48 (38.7)	390 (41.3)	
Middle	379 (35.5)	43 (34.7)	336 (35.6)	
Middle high/high	250 (23.4)	33 (26.6)	217 (23.0)	
Medical insurance, n(%)				0.421
Total/partial coverage	753 (70.4)	83 (66.9)	670 (70.9)	
No coverage	316 (29.6)	41 (33.1)	275 (29.1)	

Summary statistics are calculated based on the total number of patients without missing data.
*P value corresponding to the Wilcoxon test for the comparison of quantitative variables or to the χ^2 or Fisher's exact tests for qualitative variables, as appropriate.

Table 2 Comorbidities, clinical, laboratory and treatment characteristics according to the occurrence of herpes zoster events (HZ) in SLE patients

Variable	Total (n=1083)	HZ infection (n=125)	No HZ infection (n=958)	P value*
Manifestations at cohort entry				
Comorbidities, n (%)				
Hypertension	293 (27.2)	47 (37.6)	246 (25.8)	**0.007**
Diabetes mellitus	73 (6.7)	4 (3.2)	69 (7.2)	0.126
Malignancy	23 (2.1)	1 (0.8)	22 (2.2)	0.505
Smoking habit, n (%)	54 (28.6)	10 (33.3)	44 (27.7)	0.682
BMI, n (%)				0.506
Underweight	364 (37.7)	37 (34.3)	327 (38.2)	
Normal	414 (42.9)	46 (42.6)	368 (43.0)	
Obesity	187 (19.4)	25 (23.2)	162 (18.9)	
Fever, n (%)	446 (41.3)	55 (44.0)	391 (40.9)	0.562
Malar rash, n (%)	657 (60.7)	82 (65.6)	575 (60.1)	0.244
Discoid lupus, n (%)	88 (8.1)	16 (12.8)	72 (7.5)	0.054
Alopecia, n (%)	705 (65.3)	93 (74.4)	612 (64.1)	**0.028**
Arthritis, n (%)	874 (80.8)	93 (74.4)	781 (81.6)	0.069
Pleuritis, n (%)	278 (25.8)	35 (28.0)	243 (25.5)	0.587
Pericarditis, n (%)	193 (17.9)	21 (16.8)	172 (18.1)	0.805
Persistent proteinuria, n (%)	606 (56.2)	72 (58.1)	537 (56.2)	0.773
Cellular casts, n (%)	273 (26.6)	39 (33.6)	234 (25.7)	0.074
Psychosis, n (%)	37 (3.4)	9 (7.2)	28 (2.9)	**0.030**
Seizures, n (%)	55 (5.1)	13 (10.4)	42 (4.4)	**0.008**
Haemolytic anaemia, n (%)	129 (12.0)	17 (13.6)	112 (11.8)	0.559
Leucopenia, n (%)	494 (46.4)	64 (51.6)	430 (45.7)	0.250
Lymphopenia, n (%)	580 (54.5)	74 (60.2)	506 (53.8)	0.211
Anti-dsDNA positivity, n (%)	818 (78.0)	103 (83.1)	715 (77.3)	0.166
Lupus anticoagulant positivity, n (%)	142 (16.5)	16 (16.5)	126 (16.5)	1.000
Anti-cardiolipin positivity, n (%)	178 (19.7)	20 (19.2)	158 (19.8)	1.000
Anti-B2GPI positivity, n (%)	89 (12.2)	11 (13.9)	78 (11.9)	0.587
Low C3, n (%)	810 (76.6)	102 (81.6)	708 (75.9)	0.178
Low C4, n (%)	817 (77.6)	101 (80.8)	716 (77.2)	0.424
SDI, mean (SD)	0.67 (1.15)	0.89 (1.29)	0.64 (1.13)	**0.043**
Manifestations prior to the event				
Protein/creatinine ratio in morning urine, median (Q1–Q3)	90 (23.7–281.0)	185.0 (86.2–1172.5)	81.2 (19.9–253.7)	**0.020**
Proteinuria (g/24 hours), median (Q1–Q3)	0.32 (0.1–1.2)	0.54 (0.3–1.9)	0.30 (0.1–1.2)	**0.032**
Creatinine, median (Q1–Q3)	0.77 (0.63–0.95)	0.78 (0.69–0.90)	0.77 (0.63–0.96)	0.806
SLEDAI-2K, mean (SD)	4.4 (5.6)	6.1 (6.7)	4.2 (5.4)	**0.007**
Treatments prior to HZ event				
Antimalarials, n (%)	1023 (94.5)	105 (84.0)	918 (95.8)	**0.001**
Prednisone, mg/day (orally), median (Q1–Q2)	10 (5.91–17.5)	15.0 (5.8–30.0)	8.6 (5.9–11.7)	**0.001**
Methylprednisolone boluses, n (%)	146 (13.5)	13 (10.4)	133 (13.9)	0.331
Intravenous cyclophosphamide, n (%)	404 (37.3)	43 (34.4)	361 (37.7)	0.493
Azathioprine, n (%)	520 (48.0)	58 (46.4)	462 (48.2)	0.705
Methotrexate, n (%)	287 (26.5)	33 (26.4)	254 (26.5)	1.000

Continued

Table 2 Continued

Variable	Total (n=1083)	HZ infection (n=125)	No HZ infection (n=958)	P value*
Tacrolimus, n (%)	91 (8.4)	11 (8.8)	80 (8.3)	0.864
Ciclosporin A, n (%)	36 (3.3)	3 (2.4)	33 (3.4)	0.790
Mycophenolate mofetil, n (%)	650 (60.0)	69 (55.2)	581 (60.6)	0.246
Rituximab, n (%)	173 (15.9)	17 (13.6)	156 (16.3)	0.517
Belimumab, n (%)	81 (7.5)	10 (8.0)	71 (7.4)	0.856
Intravenous immunoglobulin, n (%)	43 (3.9)	7 (5.6)	36 (3.8)	0.327
Plasma exchange, n (%)	19 (1.7)	2 (1.6)	17 (1.8)	1.000
Multiple immunosuppressants†, n (%)	696 (64.27)	74 (59.20)	622 (64.93)	0.234

Summary statistics are calculated based on the total number of patients without missing data.
Bold values indicate statistically significant p values (p<0.05).
*P values correspond to the Wilcoxon test for the comparison of quantitative variables or to the χ^2 or Fisher's exact tests for qualitative variables, as appropriate.
†Two or more.
BMI, body mass index; C3, complement 3; C4, complement 4; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; β2GPI, beta-2 glycoprotein I.

at cohort entry as measured by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index than patients without it (mean (SD) 0.89 (1.29) vs 0.64 (1.13), p=0.043). Also, a significantly higher frequency of hypertension was found in patients with HZ infection (37.6% vs 25.8%, p=0.007) than in patients without it.

Before the HZ event, patients had a higher disease activity, as measured by SLEDAI-2K (mean (SD) 6.1 (6.7) vs 4.2 (5.8), respectively, p=0.007), and also exhibited greater renal involvement, with significantly higher median (IQR) morning urine protein/creatinine ratio compared with those without HZ (185.0 (86.2–1172.5) vs 81.2 (19.9–253.7); p=0.020), as well as a higher median (IQR) 24-hour proteinuria (in grams) (0.54 (0.3–1.9) vs 0.30 (0.1–1.2); p=0.032). Regarding SLE treatments, a higher use of antimalarials was observed in patients without HZ events (95.8% vs 84%; p=0.001). In addition, patients with HZ infection used a higher daily dose of oral prednisone prior to the event (mean (SD) 15.0 (5.8–30.0) vs 8.6 (5.9–11.7); p=0.001) than patients without such a history. No association was observed between concurrent immunosuppressive therapy or the use of multiple immunosuppressive agents and HZ occurrence.

Characteristics of HZ events in SLE patients

Of the total number of HZ infection events, the characteristics of the first event at presentation were recorded in 96 cases (table 3). The mean duration of the first HZ event was 13.3 days (SD 6.8), with a median time from SLE diagnosis to HZ infection of 69.9 (IQR 14.2–158.4) months. The most frequently involved site for the skin lesions was the thoracic region in 50 (52.1%) patients, followed by the lumbar region in 20 (20.8%) and the sacrum in 14 (14.6%). The diagnosis of HZ infection was made by the physician in 76.0% of the cases; 65.6% of the patients had unimetameric involvement and 34.4% had multimetameric. The large majority of the patients, 84.4%, received treatment with acyclovir, while the remaining 14.6% received valacyclovir. Complications occurred in 12.5% of the patients, 5.2% had superimposed bacterial infections and 11.5% presented with PHN. A second recurrent event occurred in seven (7.3%) patients and a third one in three patients (3.1%); all after SLE diagnosis. The thoracic region was the most frequently involved (71.4%) in the second event and the sacral region (66.7%) in the third. HZ occurred in 36 patients who had previously received the varicella vaccine, a live attenuated vaccine intended to prevent primary VZV infection. None of the patients was recorded as having received a live attenuated vaccine (Zostavax). A total of 18 patients were documented as having received the recombinant subunit vaccine (Shingrix), among them, 11 had a history of HZ prior to vaccination and 7 had no documented HZ events.

Among patients with HZ infection, hospitalisation data were available for 104 of them; 22 (21.2%) required hospitalisation due to this infection. Compared with non-hospitalised patients, those who were hospitalised had a significantly higher frequency of lumbar involvement (45.5% vs 12.2%, p=0.001), multimetameric involvement (59.1% vs 24.7%, p=0.005) and complications (27.3% vs 7.3%, p=0.026). In addition, they were receiving a higher median daily dose of prednisone (20.0 mg (Q1–Q3: 11.3–25.0) vs 10.0 mg (5.0–20.0), p=0.005) (table 4).

Figure 1 shows the cumulative probability of developing HZ over time based on Kaplan-Meier estimates. The cumulative incidence of HZ increased progressively over time, reaching 6.4% at 6 years and 11.7% at 12 years. The 95% CIs are represented by the shaded area that widened over time.

Table 3 Clinical features, treatments and complications of herpes zoster (HZ) events in SLE patients

Variable	First HZ event (n=96)	Second HZ event (n=7)	Third HZ event (n=3)
Duration of event, (days), mean (SD)	13.3 (6.8)	9.7 (5.8)	4.7 (2.1)
Event after SLE diagnosis, n (%)	89 (94.7)	7 (100)	3 (100)
Time since SLE diagnosis, (months), median (Q1–Q3)	69.9 (14.2–158.4)	83.2 (50.1–107.3)	127.4 (112.4–162.1)
Region involved, n (%)			
Thoracic	50 (52.1)	5 (71.4)	1 (33.3)
Lumbar	20 (20.8)	0 (0.0)	0 (0.0)
Sacral	14 (14.6)	1 (14.3)	2 (66.7)
Cervical	9 (9.4)	0 (0.0)	0 (0.0)
Cranial	6 (6.2)	1 (14.3)	0 (0.0)
Otic	3 (3.1)	0 (0.0)	0 (0.0)
Ophthalmic	5 (5.2)	0 (0.0)	0 (0.0)
Other	15 (15.6)	0 (0.0)	0 (0.0)
Localisation, n (%)			
Multimetameric	32 (34.4)	1 (14.3)	0 (0.0)
Unimetameric	61 (65.6)	6 (85.7)	3 (100)
Pain—VAS			
Median (Q1–Q3)	8.0 (5.5–9.0)	6.0 (5.0–7.0)	2.5 (1.8–3.2)
Pruritus—VAS			
Median (Q1–Q3)	5.0 (0.5–8.0)	4.0 (4.0–6.0)	3.0 (2.5–3.5)
Dysesthesias—VAS			
Median (Q1–Q3)	5.0 (2.0–7.0)	5.0 (0.0–5.0)	0.0 (0.0–0.0)
Diagnosed by physician, n (%)	73 (76.0)	6 (85.7)	2 (66.7)
Treatment, n (%)			
Acyclovir	81 (84.4)	7 (100)	2 (66.7)
Valacyclovir	14 (14.6)	0 (0.0)	0 (0.0)
Other	28 (29.2)	0 (0.0)	0 (0.0)
Complications, n (%)	12 (12.5)	0 (0.0)	0 (0.0)
Bacterial infections	5 (5.2)	0 (0.0)	0 (0.0)
Postherpetic neuralgia	11 (11.5)	0 (0.0)	0 (0.0)
Hospitalisation for HZ infection	21 (21.9)	1 (14.3)	0 (0.0)

Summary statistics are calculated based on the total number of patients with no missing data for each variable.
VAS, Visual Analog Scale.

Multivariate models

Logistic regression analyses of the probability of at least one HZ event after SLE diagnosis were performed (table 5). In the univariate analysis, hypertension (OR 1.73 (95% CI 1.17 to 2.56); p=0.006), higher disease activity as measured by SLEDAI-2K (OR 1.05 (95% CI 1.02 to 1.08); p=0.002) and the use of higher doses of prednisone (mg/day) (OR 1.11 (95% CI 1.07 to 1.15); p=<0.001) prior to the event were found to be associated with a higher HZ infection risk. Conversely, Mestizo ethnicity, relative to Caucasian, decreased the HZ infection risk (OR 0.65 (95% CI 0.43 to 0.98), p=0.040) as did the presence of low complement levels (OR 0.46 (95% CI 0.30 to 0.70), p=<0.001). In the multivariable analysis, higher disease activity (OR 1.09 (95% CI 1.02 to 1.17), p=0.015) and higher prednisone doses (OR 1.10 (95% CI 1.06 to 1.15), p<0.001) remained significantly associated with HZ risk. Additionally, female sex (OR 4.38 (95% CI 1.10 to 17.49), p=0.037) also reached statistical significance. Although hypertension and low complement were significant in the univariate analysis, their associations were not retained in the multivariate models after adjustment for SLEDAI-2K and corticosteroid use (p=0.114 and p=0.334, respectively).

Table 4 Hospitalisation for herpes zoster (HZ) events in SLE patients

Variable	No (n=82)	Yes (n=22)	P value*
Female sex, n (%)	78 (95.1)	20 (90.9)	0.604
Age at diagnosis (years), median (Q1–Q3)	26.5 (18.8–35.2)	23.9 (20.7–36.3)	0.877
Age at HZ infection (years)	35.0 (25.0–44.8)	34.0 (26.0–40.8)	0.553
Education level (years), median (Q1–Q3)	13.0 (10.0–15.2)	13.0 (11.2–16.8)	0.437
Ethnicity, n (%)			0.245
Mestizo	48 (58.5)	10 (45.5)	
White	25 (30.5)	7 (31.8)	
African Latin American	7 (8.5)	5 (22.7)	
Socioeconomic status, n (%)			0.501
Low/middle low	32 (39.5)	10 (45.5)	
Middle	29 (35.8)	5 (22.7)	
Middle high/high	20 (24.7)	7 (31.8)	
Region involved, n (%)			
Thoracic	46 (56.1)	10 (45.5)	0.517
Lumbar	10 (12.2)	10 (45.5)	**0.001**
Sacral	11 (13.4)	6 (27.3)	0.216
Cervical	7 (8.5)	2 (9.1)	1.000
Cranial	3 (3.7)	4 (18.2)	0.053
Optic	2 (2.4)	1 (4.5)	1.000
Loclaisation, n (%)			**0.005**
Multimetameric	20 (24.7)	13 (59.1)	
Unimetameric	61 (75.3)	9 (40.9)	
Pain—VAS	7 (5-9)	7 (5-9)	0.052
Pruritus—VAS	5 (2-8)	5 (2-8)	0.918
Dysesthesias—VAS	5 (2-7)	5 (2-7)	0.970
Diagnosed by physician, n (%)	61 (76.2)	20 (90.9)	0.227
Complications*, n (%)	6 (7.3)	6 (27.3)	**0.026**
SLE treatment			
Prednisone mg/day (orally), (median Q1–Q2)	10 (5.0–20.0)	20 (11.3–25.0)	**0.005**
Antimalarials, n (%)	56 (88.9)	20 (95.2)	0.668
Azathioprine, n (%)	18 (27.7)	5 (23.8)	0.947
Mycophenolate mofetil, n (%)	30 (46.2)	6 (28.6)	0.244
Cyclophosphamide, n (%)	6 (9.4)	2 (9.5)	1.000
Belimumab, n (%)	1 (1.6)	0 (0.0)	1.000
Rituximab, n (%)	3 (4.8)	2 (9.5)	0.790
Methotrexate, n (%)	4 (6.3)	2 (9.5)	1.000

Summary statistics are calculated based on the total number of patients with no missing data for each variable.
Bold values indicate statistically significant p values (p<0.05).
*Bacterial infection, postherpetic neuralgia.
VAS, Visual Analog Scale.

A Cox proportional hazards model was used to identify factors associated with the time to HZ infection onset in these patients (table 6). Older age at diagnosis (HR 1.02 (95% CI 1.01 to 1.04) p=0.027), the presence of psychosis (HR 2.22, (95% CI 1.04 to 4.72) p=0.039), a higher disease activity as measured by the SLEDAI-2K (HR 1.05 (95% CI 1.01,1.08); p=0.007) and higher daily prednisone dose (HR 1.04, (95% CI 1.03 to 1.05) p=0.001) prior to the event were significantly associated with a shorter time to the development of this infection. Although

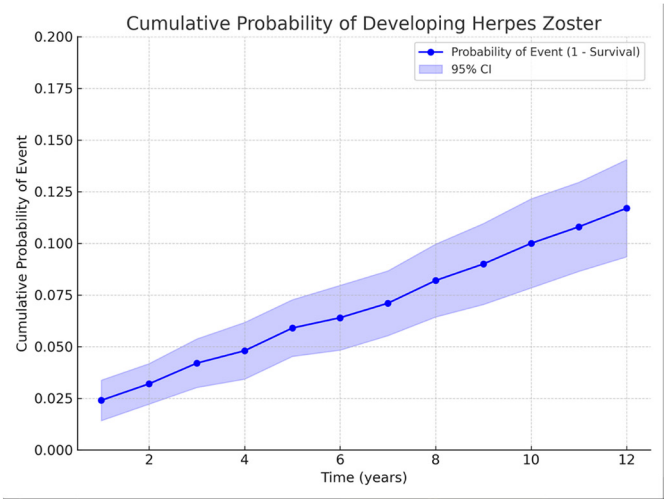

Figure 1 Kaplan-Meier cumulative risk for the first herpes zoster event in SLE patients.

low complement and azathioprine were significant in the univariate analysis, their associations were not retained in the multivariate models after adjustment for SLEDAI-2K and corticosteroid use (p=0.674 and p=0.982, respectively).

Antimalarial use could not be included in the multivariable logistic regression or Cox models because it was nearly universally used in the cohort (>94%), and the limited variability and small number of non-users precluded reliable estimation of model coefficients.

A sensitivity analysis was performed for both the logistic regression and Cox models after excluding patients who had experienced HZ events prior to cohort entry. The detailed results (online supplemental Tables 1 and 2) confirmed that disease activity, as assessed by the SLEDAI-2K, remained consistently associated with incident HZ events (p=0.004 and p=0.001, respectively).

DISCUSSION

This study provides a comprehensive evaluation of HZ infection in SLE patients from the largest multiethnic and multinational Latin American cohort, GLADEL 2.0, offering insights into both its burden and determinants of their occurrence in this population. Our findings reinforce the role of disease activity and GC exposure as

Table 5 Logistic regression model: at least one herpes zoster event from diagnosis to the end of follow-up in SLE patients

	Univariate model		Multivariate model	
Variable	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Female sex	1.57 (0.77 to 3.19)	0.212	4.38 (1.10 to 17.49)	**0.037**
Age (at diagnosis)	0.99 (0.97 to 1.00)	0.180	1.01 (0.98 to 1.04)	0.470
Ethnic group				
Caucasian	Ref		Ref	
African-Latin American	0.72 (0.34 to 1.50)	0.381	1.03 (0.25 to 4.23)	0.964
Mestizo	0.65 (0.43 to 0.98)	**0.040**	1.30 (0.67 to 2.51)	0.431
Other	2.16 (0.55 to 8.47)	0.270		
Hypertension	1.73 (1.17 to 2.56)	**0.006**		
Leucopenia	0.80 (0.55 to 1.16)	0.231		
Lymphopenia	0.75 (0.51 to 1.09)	0.132		
Proteinuria	0.99 (0.94 to 1.05)	0.815		
Low complement	0.46 (0.30 to 0.70)	**<0.001**		
SDI≥1	1.33 (0.88 to 2.02)	0.175		
SLEDAI-2K*	1.05 (1.02 to 1.08)	**0.002**	1.09 (1.02 to 1.17)	**0.015**
Prednisone (orally)*	1.11 (1.07 to 1.15)	**<0.001**	1.10 (1.06 to 1.15)	**<0.001**
Methylprednisolone boluses*	0.72 (0.39 to 1.31)	0.285		
Intravenous cyclophosphamide*	0.87 (0.59 to 1.28)	0.476		
Methotrexate*	0.99 (0.65 to 1.52)	0.978		
Azathioprine*	0.93 (0.64 to 1.35)	0.701		
Mycophenolate mofetil*	0.80 (0.55 to 1.16)	0.243		
Rituximab*	0.81 (0.47 to 1.39)	0.442		

Bold values indicate statistically significant p values (p<0.05).
*Prior to the event.
SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

Table 6 Cox models: time from diagnosis to the first herpes zoster event in SLE patients

	Univariate model		Multivariate model	
Variable	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Female sex	1.21 (0.61 to 2.39)	0.580	1.26 (0.55 to 2.9)	0.586
Age (at diagnosis)	1.01 (0.99 to 1.02)	0.447	1.02 (1.01 to 1.04)	**0.027**
Ethnic group				
Caucasian	Ref.		Ref.	
African-Latin American	0.90 (0.45 to 1.79)	0.754	1.15 (0.53 to 2.47)	0.728
Mestizo	0.79 (0.54 to 1.16)	0.226	1.10 (0.70 to 1.74)	0.679
Other	1.63 (0.49 to 5.46)	0.429	0.82 (0.16 to 4.11)	0.811
Hypertension	1.27 (0.88 to 1.83)	0.202		
Psychosis	1.81 (0.88 to 3.71)	0.104	2.22 (1.04 to 4.72)	**0.039**
Persistent proteinuria	1.00 (0.97 to 1.04)	0.831		
Leucopenia	0.79 (0.56 to 1.12)	0.192		
Lymphopenia	0.78 (0.54 to 1.11)	0.162		
Low complement	0.55 (0.37 to 0.81)	**0.003**		
SLEDAI-2K*	1.08 (1.05 to 1.11)	**0.001**	1.05 (1.01 to 1.08)	**0.007**
SDI≥1	0.93 (0.62 to 1.39)	0.726		
Prednisone mg/day (orally)*	1.04 (1.03 to 1.06)	**0.001**	1.04 (1.03 to 1.05)	**0.001**
Methylprednisolone boluses*	1.04 (0.58 to 1.85)	0.903		
Intravenous cyclophosphamide*	0.74 (0.51 to 1.07)	0.111		
Methotrexate*	0.94 (0.63 to 1.40)	0.766		
Azathioprine*	0.74 (0.52 to 1.06)	0.099		
Mycophenolate mofetil*	0.90 (0.63 to 1.29)	0.566		
Rituximab*	0.80 (0.48 to 1.35)	0.409		

Bold values indicate statistically significant p values (p<0.05).
*Prior to the event.
SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

major drivers of HZ risk, while also highlighting certain clinical features, such as NP involvement and older age at diagnosis, that may accelerate its onset.

These observations are consistent with previous reports, which have generally shown HZ prevalence of approximately 3.6% with an incidence rate between 1.2 and 4.9 cases per 1000 person-years.[3 17–19] However, Kwan *et al* in a recent Toronto Lupus Clinic cohort using a patient-reported questionnaire found higher prevalence and incidence (prevalence 30.5% and incidence of 14.3 cases per 1000 person-years) than in our cohort,[4] suggesting that methodological differences, disease severity or healthcare access may influence reported rates. Nevertheless, in a cohort from Brazil, Borba *et al* described that 4.45% of 1145 lupus patients had a total of 55 episodes of HZ, with an annual incidence rate of 6.4 events/1000 patient-years.[10]

Recurrent HZ infections are more often observed in the elderly and in immunocompromised individuals, including those with malignancies, AIDS and autoimmune diseases such as RA and SLE.[3 6 10] HZ infection recurrence in the GLADEL 2.0 cohort occurred in 21 patients (16.8%), representing a recurrence rate of 0.59×1000 person-years. This recurrence was slightly lower than rates reported in other cohorts.[4 19]

Demographic analysis of our cohort provides additional context for these findings. Overall, 89.6% of the evaluated patients were women and Mestizo (or subjects of Amerindian and European ancestry) represented the predominant ethnic group across the entire cohort. No differences were found in sex, age at diagnosis, education level and sociodemographic characteristics between patients with and without HZ infection. Although not statistically significant, differences in ethnicity were noted between groups: there was a higher proportion of White individuals (32.8% vs 24.7%) but a lower proportion of Mestizos (56.8% vs 66.0%) among those with HZ infection. This contrasts with data from the Toronto Lupus Clinic where a higher proportion of Caucasians was observed among those with HZ infection,[4] although this study did not include Mestizo individuals, limiting direct comparisons.

In the present cohort, patients with HZ infection exhibited significant differences in certain clinical

characteristics, as well as a higher frequency of cutaneous involvement such as alopecia (74.4% vs 64.1%) and neurological manifestations such as seizures (10.4% vs 4.4%) and psychosis (7.2% vs 2.9%) compared with patients without HZ infection. These findings support the role of higher disease activity and severity in increasing susceptibility to HZ. Hypertension was more frequent among patients with HZ in the descriptive and univariate analyses, but this association was not retained in the multivariable models. Notably, 64% of hypertensive patients had a history of lupus nephritis (LN), suggesting that renal involvement may partially account for this finding. Moreover, patients who developed HZ had greater cumulative damage at cohort entry and higher disease activity as measured by the SLEDAI-2K prior to the event. However, findings from other cohorts have varied, with some reporting significant associations between HZ events and musculoskeletal manifestations[4] while others found no relationship between HZ infection and any specific SLE clinical manifestations.[10] When assessing renal involvement prior to HZ events among participants in this cohort, we found that patients with HZ events had higher proteinuria compared with those without HZ. Similarly, Mok *et al* reported that HZ reactivation was common among patients with LN. In their study, at 2 years of treatment, 18% of LN episodes were complicated by HZ infection (incidence 8.84/100 patient-years). Patients with HZ reactivation, compared with those without it, were more likely to have first-time renal disease and shorter duration of LN than those without it.[20]

Treatment exposure may also play a role. Hydroxychloroquine (HCQ) use was more frequent among patients without HZ; however, the high prevalence of its exposure in the entire cohort precluded its inclusion in the multivariable analyses; thus, no independent association could be established. This observation could be related to better disease control without the risks associated with immunosuppression; nevertheless, evidence from a recent systematic review and meta-analysis failed to demonstrate a consistent protective effect of HCQ on HZ risk.[21] Although no differences were observed in the use of immunosuppressants between patients with and without HZ infection, those who developed HZ had received higher doses of prednisone prior to the event compared with those who did not. A Brazilian study reported that medication use, particularly the concomitant administration of corticosteroids and immunosuppressants, was the primary trigger for HZ infection in SLE patients, rather than disease activity.[10] Our findings partially align with these observations but also suggest that HZ risk in SLE may result from an interplay between treatment-related factors and disease activity.

The characteristics of the HZ events found in our cohort are broadly consistent with those described in the literature.[3] Most HZ infections occurred within the first 5 years after SLE diagnosis, with the thoracic region being the most frequently affected area, followed by the lumbar region. Notably, more than one-third of patients had multimetameric involvement, a pattern associated with greater HZ severity. Over 12% of patients developed complications, with PHN being the most frequent. Additionally, over 20% of patients required hospitalisation due to HZ infection. Hospitalised cases were characterised by more frequent lumbar involvement, multimetameric extension and higher complication rates, and they also received higher prednisone doses prior to the event compared with non-hospitalised patients. Although lumbar involvement was more frequently observed among hospitalised patients, when information on the reason for hospitalisation was available, hospitalisations were mainly related to extensive HZ involvement or secondary superinfections. This pattern highlights the substantial morbidity HZ imposes in patients with SLE.

In line with previous reports,[4] the Kaplan-Meier curve in our cohort showed a progressive increase in the probability of HZ over time, with the highest incidence occurring in the first year. Although the incidence declined thereafter, new cases continued to appear, indicating a cumulative risk over time. This temporal distribution reinforces the need for close surveillance and early preventive strategies, particularly during the early years of disease management.

Building on these temporal and clinical patterns, we examined factors influencing HZ risk. In our cohort, female sex, higher disease activity and the use of higher daily doses of prednisone (mg/day) were associated with an increased probability of developing at least one HZ event after SLE diagnosis. Time to event analysis further identified older age at diagnosis, the presence of psychosis, higher disease activity and a higher daily dose of prednisone as predictors of earlier HZ onset. In contrast to our findings, Mok *et al*[20] found no differences in disease activity, treatment response or other clinical parameters between patients with and without HZ. However, consistent with our results, they observed a higher incidence of HZ in LN patients receiving triple therapy (prednisolone, mycophenolate mofetil (MMF) and tacrolimus), followed by prednisolone plus CYC and prednisolone plus MMF. Their analysis also linked renal involvement, higher maximum daily doses of MMF and greater cumulative dose of CYC during induction therapy with HZ reactivation. Similarly, a recent meta-analysis found that TAC plus GC was associated with the lowest HZ risk, while CYC plus GC and MMF plus GC showed higher risks.[22] Along the same lines, Zamora *et al* reported increased risk of HZ with intravenous CYC, MMF and prednisone, whereas HCQ was protective. They found no association between disease activity and HZ occurrence, suggesting a potential protective role of HCQ, an aspect not confirmed in our study.[23]

Although earlier studies identified lymphopenia as a risk factor for HZ, this association was not observed in our cohort.[3 4] These differences may be partly explained by variations in study design, patient populations, definitions of lymphopenia or the timing and intensity of immunosuppressive therapy.

This study has some limitations. The diagnosis of HZ infection was clinically established and was based on patient self-reports, although clinical validation by the investigators was performed in most of them. Viral isolation by culture or serology was not undertaken to confirm HZ infection and events occurring prior to enrolment may be subject to recall bias. In addition, vaccination data were not systematically obtained for the entire cohort, which precluded us from estimating the risk of HZ risk according to vaccine type.

The main strength of this study lies in its inclusion of a large number of Latin American patients with lupus, representing diverse ethnic backgrounds, socioeconomic and educational levels and variable disease involvement. Furthermore, the longitudinal follow-up of patients from this cohort provides a unique opportunity to more accurately identify factors associated with the occurrence and course of HZ infection.

In summary, our findings underscore that HZ infection remains a clinically significant and potentially preventable complication in SLE, with substantial morbidity reflected by hospitalisations and complications such as PHN. Identifying patients at the highest risk, particularly those with renal involvement, high disease activity and greater GC exposure, should be a priority in routine care. These results reinforce the need for proactive risk mitigation strategies, including timely recognition and management of renal disease, minimisation of GC doses and consideration of HZ vaccination during periods of disease quiescence. Implementing such measures could meaningfully reduce the burden of HZ and improve long-term outcomes in SLE.

Author affiliations
[1]Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina
[2]Hospital Escuela Eva Peron, Granadero Baigorria, Argentina
[3]GLADEL Consultant, Rosario, Argentina
[4]Hospital Italiano de Buenos Aires, Rheumatlogy Unit, Buenos Aires, Argentina
[5]Hospital Italiano de Córdoba, Córdoba, Argentina
[6]Servicio de Reumatología, Hospital Córdoba, Córdoba, Argentina
[7]Sanatorio Allende, Córdoba, Argentina
[8]Reumatology, Hospital Privado Centro Médico de Córdoba, Córdoba, Argentina
[9]Hospital San Martin de La Plata, La Plata, Argentina
[10]Sanatorio Británico SA, Rosario, Argentina
[11]Hospital Padilla, Tucumán, Argentina
[12]Hospital J.M Ramos Mejía, Buenos Aires, Argentina
[13]Instituto de Investigaciones Médicas Alfredo Lanari, Universidad de Buenos Aires, Buenos Aires, Argentina
[14]Rheumatology and Immunology Section, CEMIC, Buenos Aires, Argentina
[15]Hospital Señor del Milagro Salta, Salta, Argentina
[16]Hospital General de Agudos Dr. Juan A. Fernández, Buenos Aires, Argentina
[17]Medical School of Federal University, Goias, Brazil
[18]Rheumatology Department, Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil
[19]Universidade Federal de Pernambuco, Recife, Brazil
[20]Hospital Universitário Pedro Ernesto, Rio de Janeiro, Brazil
[21]Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil
[22]Rheumatology, Universidade de Sao Paulo Faculdade de Medicina Hospital das Clinicas, Sao Paulo, Brazil
[23]Hospital das Clinicas HCFMUSP, Faculdade de Medicina, University of São Paulo, São Paulo, Brazil
[24]Rheumatology Divison, Department of Medicine, Escola Paulista de Medicina / Universidade Federal de São Paulo, Sao Paulo, Brazil
[25]Hospital Del Salvador, Santiago, Chile
[26]Facultad de Medicina, Universidad San Sebastián, Santiago de Chile, Hospital Dr. Franco Ravera Zunino, Rancagua, Chile
[27]Clínica de la Costa, Barranquilla, Colombia
[28]Universidad Simón Bolívar Facultad de Ciencias de la Salud, Barranquilla, Colombia
[29]Fundación Valle del Lili, Universidad Icesi, Cali, Colombia
[30]Facultad de Medicina, Universidad Nacional de Colombia, Servicio de Reumatología, Hospital Universitario Fundación Santa Fe de Bogotá; Hospital Universitario Nacional de Colombia, Bogotá, Colombia
[31]Centro de Referencia en Osteoporosis & Reumatología, Cali, Colombia
[32]Pontificia Universidad Javeriana, Cali, Colombia
[33]Servicio de Reumatología, Instituto de Reumatología, Hematología y Dermatología (IRHED), Guayaquil, Ecuador
[34]Hospital de Especialidades Dr. Antonio Fraga Mouret, Mexico City, Mexico
[35]Instituto Mexicano del Seguro Social, Mexico City, Mexico
[36]Hospital de Especialidades del Centro Médico Nacional SXXI, Instituto Mexicano del Seguro Social (IMSS), Ciudad de México, Mexico
[37]Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico
[38]Departamento de Reumatología, Instituto Nacional de Cardiología "Ignacio Chávez", Ciudad de México, Mexico
[39]Centro de Estudios de Investigación Básica y Clínica, S.C, Guadalajara, Mexico
[40]Hospital Central Dr Ignacio Morones Prieto, San Luis Potosi, Mexico
[41]Internal Medicine Department and Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Mexico
[42]Universidad Nacional de Asunción Facultad de Ciencias Médicas, Asunción, Paraguay
[43]Hospital Nacional Edgardo Rebagliati Martins, Lima, Peru
[44]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistemicas, Universidad Científica del Sur, Lima, Peru
[45]Rheumatology Department, Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru
[46]Servicio de Inmunología y Reumatología, Hospital Nacional Cayetano Heredia, Universidad Peruana Cayetano Heredia, Lima, Peru
[47]Hospital Docente Padre Billini, Santo Domingo, Dominican Republic
[48]Unidad de Enfermedades Autoinmunes Sistémicas, Hospital de Clínicas, Montevideo, Uruguay
[49]Unidad de Enfermedades Autoinmunes, Médica Uruguaya, Corporación de Asistencia Médica, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay
[50]Department of Medicine, Division of Clinical Immunology and Rheumatology, School of Medicine, The University of Alabama, Birmingham, Alabama, USA

Acknowledgements The authors would like to express their sincere gratitude to Daniel F Villalba, Leonardo A Grasso, Lucas Casariego, Mauricio Zamboni and Paulo De Los Santos (ARTHROS Software, Rosario, Argentina), as well as to Leandro Cino (Grupo Latino Americano De Estudio del Lupus (GLADEL) Project Manager, Buenos Aires, Argentina), Antonela Vannucci (GLADEL Secretary, Rosario, Argentina) and Rosana Martiarena (GLADEL Secretary, Buenos Aires, Argentina), for their invaluable contributions. The authors would also like to acknowledge all patients and investigators across countries from GLADEL 2.0 for their contributions to the study.

Collaborators Grupo Latino Americano De Estudio del Lupus (GLADEL 2.0) Study group of PANLAR.

Contributors All authors were involved in drafting or revising this article critically for important intellectual content, and all authors approved the final version to be published. RN and GP-E have full access to the dataset used for the study and take responsibility for data integrity and accuracy of the analyses performed. Responsible for the overall content as a guarantor: RN and GP-E.

Funding Funding for this study was provided by GlaxoSmithKline (GSK). GSK was provided with the opportunity to review a preliminary version of this manuscript for factual accuracy, but the authors are solely responsible for the final content and interpretation.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. This study was conducted in accordance with Good Clinical Practice (GCP), as defined by the International Conference on Harmonisation and in accordance with the ethical principles of the European Union Directive 2001/20/EC and the United States Code of Federal Regulations, Title 21, Part 50 (21CFR50). This study was approved by Comité de Ética para la Investigación Clínica, Fundación Dr. J.R. Villavicencio. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

ORCID iDs
Romina Nieto https://orcid.org/0000-0002-2895-3060
Eduardo F Borba https://orcid.org/0000-0001-6194-5129
Edgard Torres dos Reis-Neto https://orcid.org/0000-0003-0657-4825
Jose Maximiliano Martinez https://orcid.org/0000-0001-7373-3027
Eduardo Martín-Nares https://orcid.org/0000-0002-7911-1269
Bernardo A Pons-Estel https://orcid.org/0000-0003-2518-0266

REFERENCES

1 Pons-Estel GJ, Alarcón GS, Scofield L, *et al*. Understanding the epidemiology and progression of systemic lupus erythematosus. *Semin Arthritis Rheum* 2010;39:257–68.
2 Chakravarty EF, Michaud K, Katz R, *et al*. Increased incidence of herpes zoster among patients with systemic lupus erythematosus. *Lupus (Los Angel)* 2013;22:238–44.
3 Chen D, Li H, Xie J, *et al*. Herpes zoster in patients with systemic lupus erythematosus: Clinical features, complications and risk factors. *Exp Ther Med* 2017;14:6222–8.
4 Kwan A, Rayes HA, Lazova T, *et al*. Herpes zoster in SLE: prevalence, incidence and risk factors. *Lupus Sci Med* 2022;9:e000574.
5 Gershon AA, Breuer J, Cohen JI, *et al*. Varicella zoster virus infection. *Nat Rev Dis Primers* 2015;1:15016.
6 Kawai K, Yawn BP. Risk Factors for Herpes Zoster: A Systematic Review and Meta-analysis. *Mayo Clin Proc* 2017;92:1806–21.
7 Steinmann M, Lampe D, Grosser J, *et al*. Risk factors for herpes zoster infections: a systematic review and meta-analysis unveiling common trends and heterogeneity patterns. *Infection* 2024;52:1009–26.
8 Gormezano NWS, Silva CA, Otsuzi CI, *et al*. Higher Prevalence and Distinct Features of Herpes Zoster Infection in Children than Adults with Systemic Lupus Erythematosus. *Pediatr Infect Dis J* 2015;34:905–7.
9 Hu SC-S, Lin C-L, Lu Y-W, *et al*. Lymphopaenia, anti-Ro/anti-RNP autoantibodies, renal involvement and cyclophosphamide use correlate with increased risk of herpes zoster in patients with systemic lupus erythematosus. *Acta Derm Venereol* 2013;93:314–8.
10 Borba EF, Ribeiro ACM, Martin P, *et al*. Incidence, risk factors, and outcome of Herpes zoster in systemic lupus erythematosus. *J Clin Rheumatol* 2010;16:119–22.
11 Gómez-Puerta JA, Pons-Estel GJ, Quintana R, *et al*. A longitudinal multiethnic study of biomarkers in systemic lupus erythematosus: Launching the GLADEL 2.0 Study Group. *Lupus (Los Angel)* 2021;30:630–40.
12 Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997;40:1725.
13 Petri M, Orbai A-M, Alarcón GS, *et al*. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2012;64:2677–86.
14 Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. *J Rheumatol* 2002;29:288–91.
15 Gladman D, Ginzler E, Goldsmith C, *et al*. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. *Arthritis Rheum* 1996;39:363–9.
16 R Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing; 2021. Available: https://www.R-project.org
17 Thomas SL, Hall AJ. What does epidemiology tell us about risk factors for herpes zoster? *Lancet Infect Dis* 2004;4:26–33.
18 Jih J-S, Chen Y-J, Lin M-W, *et al*. Epidemiological features and costs of herpes zoster in Taiwan: a national study 2000 to 2006. *Acta Derm Venereol* 2009;89:612–6.
19 Yawn BP, Saddier P, Wollan PC, *et al*. A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction. *Mayo Clin Proc* 2007;82:1341–9.
20 Mok CC, Tse SM, Chan KL, *et al*. Prevalence and risk factors of herpes zoster infection in patients with biopsy proven lupus nephritis undergoing immunosuppressive therapies. *Lupus (Los Angel)* 2020;29:836–44.
21 Wang HF, Gao Y, Lin Z, *et al*. Prevalence, incidence, and risk factors for herpes zoster in systemic lupus erythematosus: a systematic review and meta-analysis. *Front Immunol* 2025;16:1544218.
22 Jiang N, Jin S, Yu C, *et al*. Efficacy and safety of immunosuppressive agents for adults with lupus nephritis: a systematic review and network meta-analysis. *Front Immunol* 2023;14:1232244.
23 Zamora LD, Collante MTM, Navarra SV. Risk factors for herpes zoster infection among Filipinos with systemic lupus erythematosus. *Int J Rheum Dis* 2020;23:197–202.