Incidence and clinical-laboratory aspects of systemic lupus erythematosus in a Southern Brazilian city

Carlos Alberto Kenji Nakashima[1], Ana Paula Galhardo[1], Jackeline Ferreira Marinho da Silva[1], Gracielle Rodrigues Fiorenzano[1], Anelyse Bozzo da Silva dos Santos[1], Manoel Fernando Silva Leite[2], Marcio Augusto Nogueira[3], Poliana Vieira da Silva Menolli[4], Rafael Andrade Menolli[5]

ABSTRACT

Introduction: Brazilian epidemiological studies on systemic lupus erythematosus (SLE) are scarce, and currently available data originate almost entirely from international literature. Objectives: To determine the incidence and some clinical and laboratory characteristics of patients with SLE in the municipality of Cascavel, state of Paraná, Brazil. **Patients and Methods:** Data were collected from August 2007 to July 2008 in all health services of Cascavel providing health care in rheumatology: a university-affiliated hospital, a public outpatient clinic, and three private clinics. **Results:** The study identified 14 patients diagnosed with SLE, which resulted in an estimated incidence of 4.8 cases/100,000 inhabitants/year. All patients were female, and the mean age was 41.5 years. The highest incidence of disease occurred between 30 and 39 years of age, and 92.8% of patients met at least four of the 11 American College of Rheumatology (ACR) criteria for diagnosis of SLE. The drug treatment of patients was also assessed and proved to be in accordance with the Brazilian Consensus for Treatment of SLE. **Conclusion:** The incidence obtained in the municipality of Cascavel is close to those reported in international studies.

Keywords: systemic lupus erythematosus, incidence, epidemiology.

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease, characterized by the production of autoantibodies against several cell constituents.[1] Epidemiological studies of incidence and prevalence of SLE have shown varied results in different regions of the world,[2] and, within the same country, the incidence rates have also differed significantly.[3] Most studies have been carried out in European countries or in the United States of America (USA),[2] compromising the understanding of SLE epidemiology in Brazil. Such studies are scarce in Brazil,[4] which has a population with high racial and cultural miscegenation, in addition to regions with different climate conditions, which can influence the disease onset and its complications. This study aimed at assessing the incidence of SLE in the municipality of Cascavel, state of Paraná, from August 2007 to July 2008, as well as describing the clinical and laboratory characteristics of these patients.

PATIENTS AND METHODS

This is an incidence study carried out by reviewing the medical records of patients diagnosed with SLE in the municipality of Cascavel, state of Paraná, from August 2007 to July 2008. This study searched all health care services in the municipality that provided health care in rheumatology: a university-affiliated hospital (Hospital Universitário do Oeste do Paraná); a public outpatient clinic (Centro Regional de Especialidades do

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Universidade Estadual do Oeste do Paraná – UNIOESTE, Brazil.
1. Medical student at UNIOESTE
2. Rheumatologist of the UNIOESTE
3. Rheumatologist; professor of Rheumatology of the UNIOESTE
4. Master in Collective Health; Assistant professor of Collective Health of the UNIOESTE
5. Master, Assistant professor of Immunology of the UNIOESTE
Correspondence to: Rafael Andrade Menolli. Centro de Ciências Médicas e Farmacêuticas. Rua Universitária, 1619. Bairro Universitário. CEP: 85819-110. Cascavel, PR, Brazil. E-mail: ramenolli@hotmail.com

Consórcio Intermunicipal de Saúde do Oeste do Paraná); and three private clinics of rheumatology.

Data collection team actively searched the above-cited services, and the medical records of all patients diagnosed with SLE confirmed by a rheumatologist in the period studied were assessed. The patients diagnosed with SLE who did not live in the municipality were not included in the study.

The following data were collected: age group; gender; time from the first complaint until diagnosis; drug therapy; and clinical-laboratory manifestations. Compliance with the American College of Rheumatology (ACR) critera[5] and of the Third Brazilian Consensus for Autoantibodies Screening in HEp-2 Cells (FAN)[6] was assessed.

The estimated population of Cascavel for 2008 by the Brazilian Institute of Geography and Statistics (IBGE) was 291,747 inhabitants (149,790 female and 141,957 male), and these figures were used for calculating the incidence.[7]

Data were shown as frequencies, medians, and means ± standard deviation, with a 95% confidence interval.

This study was approved by the Research Ethics Committee of Universidade Estadual do Oeste do Paraná, and reports no conflict of interest.

RESULTS

Fourteen patients diagnosed with SLE were identified living in the municipality of Cascavel during the study period. Based on the IBGE estimated population for the municipality in 2008, the incidence of SLE was estimated as 4.8 cases per 100,000 inhabitants/year.

All patients were females and the incidence estimated for gender was 9.3 cases/100,000 inhabitants/year. The mean age at diagnosis was 41.5 ± 14.44 years (95% CI: 33.16 – 49.83), ranging from 22 to 69 years (median, 38 years). The incidence and frequency of SLE according to age group are shown in Table 1.

Table 1
Age group of patients diagnosed with SLE in the municipality of Cascavel between 2007 and 2008

Age group (years)	n	Frequency of cases (%)	Population*	Incidence (/100,000 inhab)
20 - 29	3	21.42	54,546	5.50
30 - 39	5	35.71	46,986	10.64
40 - 49	2	14.29	39,880	5.02
50 - 59	2	14.29	26,129	7.65
Over 60	2	14.29	23,135	8.64

* Data according to age group. Source: IBGE estimate for the municipality of Cascavel, PR, in 2008.

The time elapsed between the first complaint and diagnosis was up to six months in 57.14% (n = 8), between six months and two years in 28.56% (n = 4), and over five years in 14.29% (n = 2) of the cases. The mean time was 21.6 ± 42.8 months (95%CI: 3.13 – 46.24).

Of the 11 ACR criteria for SLE diagnosis, ten patients (71.43%) met four criteria, and four patients (21.4%) met five criteria. Table 2 shows the clinical and laboratory manifestations of patients. All patients were antinuclear antibody (ANA) positive.

Table 2
Clinical and laboratory manifestations of the 14 patients diagnosed with SLE in the municipality of Cascavel between 2007 and 2008

Criteria/ACR	n (%)
ANA	14 (100)
Arthritis	12 (85.7)
Photosensitivity	9 (64.3)
Malar rash	8 (57.1)
Hematologic disorders	7 (50)
Kidney disorders	4 (28.6)
Oral ulcer	3 (21.4)
Serositis	2 (14.3)
Immune disorders	1 (7.1)
Discoid rash	0 (0)
Neurological disorders	0 (0)

All patients had ANA titers greater than 1/160. The reading patterns found for ANA were as follows: nuclear (without specifications) in 42.85% (n = 6); homogeneous nuclear in 42.85% (n = 6); speckled nuclear in 7.15% (n = 1); and mixed (nuclear and cytoplasmic) in 7.15% (n = 1) of the cases. Data on autoantibodies, other than ANA, were not available in the medical records.

The drugs used in the pharmacological treatment are shown in Table 3. Only two patients were on monotherapy: one

Table 3
Drugs Prescribed to patients with SLE in the municipality of Cascavel, state of Paraná, between 2007 and 2008

Drugs	n (%)
Corticoids	13 (92.86)
Antimalarial drugs	6 (42.85)
Immunosuppressants	5 (35.71)
Non-steroidal anti-inflammatory drugs (NSAID)	4 (28.57)
Anti-hypertensive drugs	2 (14.28)
Discoid rash	0 (0)

with hydroxychloroquine and the other with prednisone. The remaining patients were treated with combination therapy shown in Table 4.

Table 4
Immunosuppressant/anti-inflammatory treatment prescribed to patients with SLE in the municipality of Cascavel, state of Paraná, between 2007 and 2008

Treatment	n (%)
Prednisone + Chloroquine	3 (21.43)
Prednisone + Diclofenac	2 (14.28)
Prednisone + Azathioprine	2 (14.28)
Prednisone + Methotrexate	1 (7.15)
Methylprednisolone + Chloroquine	1 (7.15)
Prednisone + Diclofenac + Azathioprine	1 (7.15)
Prednisone + Chloroquine + Azathioprine	1 (7.15)
Monotherapy	2 (14.28)

DISCUSSION

Most epidemiological data about SLE originate from countries such as the USA and England,[8,9] and literature about SLE epidemiology in Brazil is scarce. International references have reported an incidence ranging from 1.15 to 9.3 cases/100,000 inhabitants/year. The first study conducted in Brazil about the incidence of SLE in the city of Natal, state of Rio Grande do Norte, has reported 8.7 cases/100,000 inhabitants/year,[4] which is much higher than most published international data. Thus, the data from the municipality of Cascavel are in accordance with international results, but below those found in the Northeast region of Brazil. Data are shown in Table 5.

The incidence difference between Cascavel/PR and Natal/RN can be explained by the higher incidence rates of ultraviolet B radiation in the city of Natal,[10] due to its geographical position in the Northeast region of Brazil, differently from that of the municipality of Cascavel, in the Southern region.[11] Because SLE is more common in the black population,[12] other factors, such as ethnical and economic compositions, may be involved. The city of Natal has a greater percentage of mixed heritage and black individuals than the municipality of Cascavel (55.4% and 20.2%)[13] and a lower human development index (HDI).[14] Although a relationship between the incidence of SLE and economic aspects has not been found, disease survival is linked to patients' life conditions.[15]

The incidence of 4.8 cases per 100,000 inhabitants/year in the municipality of Cascavel was the same found in Sweden by Stalh-Hallengren *et al.*,[16] and very similar to the 4.71 cases/100,000 inhabitants/year reported by Somers *et al.*[17] in the United Kingdom and the 4.6 cases/100,000 inhabitants/year reported by Nossent[18] in Curacao, West Indies. However, it is greater than that observed by Siegel and Lee[19] in New York, USA, and by Hopkinson *et al.*[20] in Nottingham, United Kingdom (2.0 cases/100,000 inhabitants/year and 3.7 cases/100,000 inhabitants/year, respectively).

Table 5
International studies on incidence of SLE (cases/100,000 inhabitants)

Author, study site	Study period	Total of SLE cases (n)	Incidence (per 100,000 inhabitants)
Present study, Cascavel, Brazil	1997-1998	14	4.8
Hopkinson *et al.*[2], Nottingham, United Kingdom	1989-1990	23	3.7
Pereira Vilar and Sato,[4] Natal, RN, Brazil	2000	43	8.7
Stalh-Hallengren *et al.*,[16] South Sweden	1987-1991	41	4.8
Nossent,[18] Curaçao, West Indies	1980-1989	94	4.6
Siegel and Lee,[19] New York, USA	1956-1965	98	2.0
Govoni *et al.*,[21] North of Italy	2000-2002	299	2000 - 2.01 2001 - 1.15 2002 - 2.6
Johnson *et al.*,[22] Birmingham, United Kingdom	1991	33	3.8
Naleway *et al.*,[23] rural area, Wiscosin, USA	1991-2001	117	5.1
Lopez *et al.*,[25] Northern Spain	1992-1997	367	2.15
Uramoto *et al*[27], Rochester, MN, USA	1980-1992	48	5.5
Morton *et al*[31], North American Natives	1971-1975	75	9.3
Chiu e Lai[32], Taiwan	2007	1558	6.8

A greater incidence of SLE in women has always been reported.[8,21,22] The result for the female population in the municipality of Cascavel (9.3 cases/100,000 inhabitants/year) was lower than that in the city of Natal (14.1 cases/100,000 inhabitants/year[4]) and similar to that obtained in the United Kingdom between 1990 and 1999 (8.01 cases/100,000 inhabitants/year).[17]

In our study, the mean age of women at diagnosis (41.5 years) was higher than that found in the city of Natal[4] (31.8 years) and similar to that reported in international studies (40.6 years in the USA,[8] and 46 and 37 years in the United Kingdom[9,22]).

The peak incidence of disease occurred at ages 30 to 39 years. Most cases (71%) appeared between 20 to 49 years of age, similarly to what was found in Curacao[18] and Natal,[4] also located in developing countries, but differently from what was found in the United Kingdom,[9] whose higher incidence occurred between 60 to 69 years of age (4.71 cases/100,000 inhabitants/year), and in the rural area of Wisconsin, USA,[23] whose higher incidence occurred at the age of 60 to 79 years (11.5 cases/100,000 inhabitants/year).

In our study, the mean time required for diagnosis was 21.6 months, which was shorter when compared with the analyses performed by Hopkinson *et al.*[20] and Voss *et al.*,[24] who reported 61 months and 28.8 months, respectively. In our study, most patients were diagnosed in less than four months, which might reflect the good awareness of the health care network for diagnosing SLE.

Of the ACR criteria for diagnosing SLE, significant positive ANA titers in all patients stood out. Positive ANA titers are extremely common in SLE as shown in Spain,[25] Denmark,[24] and also Brazil[4] (positivity of 95.6%, 100%, and 100%, respectively). The titers found confirmed that patients with SLE, differently from healthy individuals, tend to have moderate to high ANA titers.[26]

The presence of arthritis, photosensitivity, and malar rash was similar to the results from Natal[4] and higher than those from the following: New York[8] and Curaçao[18] (65% of arthritis and 45% of photosensitivity, respectively); and United Kingdom, by Nightingale *et al.*[9] (9.7% of malar rash and 10.8% of photosensitivity).

The incidence of renal disorders was similar to that reported by Naleway *et al.*[23] in the rural area of Wisconsin, USA, (27.3%), and by Pereira Vilar and Sato,[4] but lower than that reported by Nossent,[18] in Curacao (48%). These differences can be explained by the time required for diagnosis: renal disorders appear in up to 75% of the patients with confirmed diagnosis for at least five years;[8] thus, in an early diagnosis, renal disorder might not have appeared yet.

The ACR criteria presented by SLE patients were very similar in both Brazilian studies, differences being observed in the immunological disorders (54% in Natal, and 7.1% in Cascavel) and in the discoid rash (37% in Natal, and 0% in Cascavel). The result regarding the immunological disorders in the municipality of Cascavel is very different from those obtained in other studies,[16,23,24] and it might have been due to problems in recording data in the medical records, considering that immune disorders are common in SLE.[27]

Regarding drug treatment for SLE, the patients from Cascavel used mainly corticosteroids, which are the most commonly used anti-inflammatory drugs in different populations. Uramoto *et al.*[27], assessing the medical records of patients for more than 40 years in the USA, have reported the use of corticosteroids in 62% of patients between 1950 and 1979, and a decrease in their use (48%) between 1980 and 1992.

The drug treatment of patients from Cascavel is in accordance with the Brazilian Consensus for Treatment of SLE,[28] which identifies corticosteroids and antimalarial drugs as the most used treatment for the disease. It also indicates the association of corticosteroids with other drugs, such as antimalarials and immunosuppressants, azathioprine and methotrexate. Such associations were evidenced in this study, where 12 (85.7%) of the 14 patients were on a multidrug treatment.

The municipality of Cascavel showed lower incidence data than those reported in the only previous publication in Brazil, but similar to those of European and North-American studies. This raises questions about the environmental influence (socioeconomic and racial) as the fundamental factor for SLE emergence and patients' survival.[15]

Epidemiological surveys reflecting regional differences are of great importance for a country of continental dimensions, such as Brazil.[29] The attained information may determine more adequate approaches for managing patients of different ethnicities, and socioeconomic and environmental conditions, and for organizing health services.[30]

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