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Mortality from systemic erythematosus lupus in Brazil: evaluation of causes according to the government health database[☆]



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ABSTRACT

Objective: To characterize the causes of mortality in patients with systemic lupus erythematosus (SLE) in Brazil between 2002 and 2011.

Methods: An exploratory ecological study of a time series using data from the Mortality Information System of DATASUS, the Department of the Unified Health System (Brazil's National Health System).

Results: Brazil's SLE mortality rate was 4.76 deaths/10⁵ inhabitants. The mortality rate was higher in the Midwest, North and Southeast regions than in the country as a whole. There were 6.3% fewer and 4.2% more deaths than expected in the Northeast and Southeast regions, respectively. The mean age at death was 40.7 ± 18 years, and 45.61% of deaths occurred between the ages of 20 and 39. Incidence was highest in women (90.7%) and whites (49.2%). Disorders of the musculoskeletal system and connective tissue were mentioned as an underlying cause of death in 77.5% of cases, and diseases of the circulatory system and infectious and parasitic diseases were also noted in fewer cases. SLE was mentioned as an underlying cause of death in 77% of cases, with no difference between the Brazilian regions ($p = 0.2058$). The main SLE-related causes of death were, sequentially, diseases of the respiratory and circulatory systems and infectious and parasitic diseases.

Conclusions: This study identified a need for greater control of risk factors for cardiovascular diseases and a better understanding of the pathogenesis of atherosclerosis in SLE. Infectious causes are still frequent, and management should be improved, especially in the early stages of the disease.

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Mortalidade por lúpus eritematoso sistêmico no Brasil: avaliação das causas de acordo com o banco de dados de saúde do governo

R E S U M O

Palavras-chave:

Lúpus eritematoso sistêmico
Mortalidade
Brasil

Objetivo: Caracterizar as causas de mortalidade em pacientes com lúpus eritematoso sistêmico (LES) no Brasil entre 2002 e 2011.

Métodos: Estudo ecológico exploratório de uma série cronológica com dados do Sistema de Informações sobre Mortalidade do Departamento de Informática do Sistema Único de Saúde (Datasus).

Resultados: A taxa de mortalidade por LES no Brasil foi de 4,76 mortes/105 habitantes. A taxa de mortalidade foi maior nas regiões Centro-Oeste, Norte e Sudeste do que no país como um todo. Houve 6,3% menos e 4,2% mais mortes do que o esperado nas regiões Nordeste e Sudeste, respectivamente. A média de idade ao óbito foi de $40,7 \pm 18$ anos e 45,61% dos óbitos ocorreram entre 20 e 39 anos. A incidência foi maior nas mulheres (90,7%) e nos brancos (49,2%). Os distúrbios do sistema musculoesquelético e do tecido conjuntivo foram mencionados como a causa subjacente de morte em 77,5% dos casos; também foram observadas doenças do sistema circulatório e infecciosas e parasitárias, embora em menor frequência. O LES foi mencionado como a causa subjacente de óbito em 77% dos casos, sem diferença entre as regiões brasileiras ($p=0,2058$). As principais causas de morte associadas ao LES foram, em ordem, doenças dos sistemas respiratório e circulatório e doenças infecciosas e parasitárias.

Conclusões: Este estudo identificou a necessidade de maior controle dos fatores de risco para doenças cardiovasculares e uma melhor compreensão da patogênese da aterosclerose no LES. As causas infecciosas ainda são frequentes e o manejo deve ser melhorado, especialmente nos estágios iniciais da doença.

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Introduction

Systemic lupus erythematosus (SLE), a chronic autoimmune disease whose etiology is not fully known, is diagnosed based on clinical and laboratory criteria and probably results from the interaction of genetic, hormonal, environmental and infectious factors that lead to the loss of immunological tolerance with the production of autoantibodies.¹

According to the literature, mortality in SLE follows a bimodal pattern: in the early stages, death is mainly caused by infection, followed by severe renal or central nervous system (CNS) activity, while in the more advanced stages of the disease, there is an increase in mortality from cardiovascular diseases associated with atherosclerosis, partially related to corticotherapy and chronic inflammation.^{1,2}

According to the Ministry of Health, the death certificate is the standard document for collecting information on mortality and is the source of vital and epidemiological statistics in Brazil.³ The causes of death to be registered on the international death certificate are all those diseases, morbid conditions or injuries that either resulted in or contributed to death and the circumstances of the accident or violence that produced any such injuries. Underlying Cause of Death is defined as the disease or injury that initiated the train of morbid events leading directly to death.³

The Conditions and Causes of Death section of the death certificate is in accordance with the international

death certificate model adopted by the World Health Organization (WHO), which is extremely important given that it contains the underlying cause and injuries leading to death. It is divided into two parts. Part I is for reporting the direct cause of death (immediate cause – line A) and the morbid conditions that led to the cause registered in line A (antecedent or sequential causes – lines B and C, and the underlying cause – line D). Part II is for reporting contributing causes that were not part of the chain defined in Part I, including any diseases or injuries that contributed to death but were not directly related to the pathological state leading to death.³

In Brazil, with its size and the different levels of socioeconomic development in its various regions, as well as the different levels of organization and problem-solving capabilities of health assistance networks, the causes of mortality may vary according to region and may reflect differences in care and access to health services between regions. This study therefore aims to determine the causes of mortality in SLE patients in Brazil, according to region, from 2002 to 2011.

Patients and methods

An exploratory ecological study of a time series of 8761 deaths in which SLE was recorded as the underlying or a sequential cause of death was conducted. The data were collected from the File Transfer Protocol of the Mortality Information System (SIM) of the IT Department of the Unified Health System

(DATASUS),⁴ which is why it was not necessary to submit this study to the Human Research Ethics Committee for approval. The database was prepared using TabWin[®].

The selected variables were the region where the patient lives (North, Northeast, Midwest, South and Southeast), gender (male or female), race (mixed race, white, black, east Asian and indigenous), age and underlying and sequential causes of death recorded in the years of the historical series.

This study considered as the underlying cause of death all the causes of death registered as such in accordance with the Tenth Revision of the International Classification of Diseases (ICD-10) and available in DATASUS.

SLE is a disease described in Chapter XIII of ICD-10, called "Diseases of the Musculoskeletal System and Connective Tissue" (M00 to M99).⁵

The data collected included information from the death certificates of patients aged 15 and over and whose Part I (lines, a, b, c and d) or II of the Conditions and Causes of Death section included disease M32 - SLE and its sub-categories (M32.0 - Drug-induced systemic lupus erythematosus M32.1 - Systemic lupus erythematosus with organ or system involvement; M32.8 - Other forms of systemic lupus erythematosus; and M32.9 - Systemic lupus erythematosus, unspecified).⁵ Death certificates that did not mention age were excluded.

The populations of the states and regions as disclosed by DATASUS, which are based on census and intercensus data published by the Brazilian Institute of Geography and Statistics (IBGE),⁶ were used to calculate the incidence rate, while the average population in the two middle years of the studied period (2006 and 2007) was used to calculate the average incidence in the period.

Statistical analysis was carried out using descriptive and inferential statistical methods. The number of expected deaths for each region was calculated by assuming the average Brazilian population in the historical series as the standard population under absolute risk in each region. Quantitative variables had an average standard deviation of ± 1.96 , were submitted to the D'Agostino normality test and were compared using the Z test. Qualitative variables were analyzed in terms of absolute and relative frequencies, and their distribution was evaluated using the Chi-square test. A significance level of $\alpha < 5\%$ was established beforehand to reject the null hypothesis. Statistical processing was performed using BioEstat[®] version 5.3 and GrafTable[®] version 2.0.

Table 2 – Distribution by gender, race and age at death of patients with systemic lupus erythematosus in Brazil between 2002 and 2011.

Variables	n = 8761	%
Gender		
Male	812	9.3
Female	7949	90.7 ^a
Race		
White	4310	49.2 ^a
Mixed race	2917	33.3
Black	815	9.3
Yellow	44	0.5
Indigenous	9	0.1
Not reported	666	7.6
Age		
15–19	789	9.01
20–39	3996	45.61 ^a
40–59	2888	32.96
60–79	955	10.90
80 and over	133	1.52

Source: Mortality Information System (SIM) of the IT Department of the Unified Health System – DATASUS.

^a p -Value < 0.0001 , Chi-square test of goodness of fit.

Results

This study identified 8761 reports of deaths of SLE patients in Brazil, giving a specific mortality rate of 4.76 deaths/ 10^5 inhabitants. The Midwest, North and Southeast regions had rates of 6.44, 5.4 and 5.23 deaths/ 10^5 inhabitants, respectively, which were above the Brazilian average. The lowest rate of mortality from SLE was found in the Northeast region (3.69/ 10^5 inhabitants), and the present study identified a statistically significant difference ($p < 0.0001$) of 6.3% fewer deaths than expected in this region, while the Southeast region had 4.2% more deaths than expected ($p < 0.0001$) (Table 1).

Table 2 shows a significant predominance ($p < 0.0001$) of women (90.7%), whites (49.2%) and those aged between 20 and 39 years (45.61%).

Between 2002 and 2011, the national mean age at death was 40.7 ± 18 years, with significant differences from this mean ($p < 0.0001$) in the North (34.1 ± 13.7 years) and South

Table 1 – Distribution of observed and expected deaths of patients with systemic lupus erythematosus by region between 2002 and 2011.

Region	Deaths/100,000 inhabitants	Observed deaths (n)	Observed (%)	Expected (%)	Dif. (%)
Brazil	4.76	8761	100.0	100.0	0.0
North	5.40	789	9.0	7.9	1.1
Northeast	3.69	1902	21.7	28.0	-6.3 ^a
Southeast	5.23	4076	46.5	42.3	4.2 ^a
South	4.28	1143	13.0	14.5	-1.5
Midwest	6.44	851	9.7	7.2	2.5

Source: Mortality Information System (SIM) of the IT Department of the Unified Health System – DATASUS.

^a p -Value < 0.0001 , Chi-square test.

(44.7 ± 17 years) regions. In the Northeast, Southeast and Midwest regions, the means age at death were 37.1 ± 15.1 years, 42.9 ± 20 years and 38.8 ± 15.3 years, respectively.

In SLE patients, the ICD-10 group “Disorders of the Musculoskeletal System and Connective Tissue” (6794) accounted for 77.5% of underlying causes of death, with a statistically significant difference ($p < 0.0001$) in relation to the other recorded underlying causes of death in these patients. SLE (M32), as one of the diseases that is part of this ICD-10 group, represented approximately 100% (6745) of all records of underlying cause of death in this group. SLE alone accounted for 77% of records of underlying cause of death (6745/8761) among the total number of deaths of patients with this disease. There was not a statistically significant difference ($p = 0.2058$) between the percentage of deaths classified as M32 among the Brazilian regions (Table 3).

Other underlying causes of death recorded for SLE patients included circulatory system (6.0%), infectious and parasitic

(2.8%), respiratory system (2.2%), digestive system (2.1%) and genitourinary system (1.9%) diseases (Table 3).

Table 3 shows that the predominance of records was not uniform across the regions except for those related to the circulatory system and infectious and parasitic diseases. Although the Southeast region had the lowest percentage of cases of SLE with SLE as the underlying cause of death (74.3% = 3030/4076), it accounted for 46.5% (4076/8761) of total deaths of SLE patients in the country, as well as the highest proportion of most conditions recorded as the underlying cause of death.

The distribution of sequential causes of death related to SLE (Table 4) showed highly significant differences ($p < 0.0001$) for respiratory system (26.4%), circulatory system (20.7%), infectious and parasitic (18.9%) and genitourinary system (14.7%) diseases.

The comparison of sequential causes between regions (Table 5) showed a predominance of diseases of the respiratory

Table 3 – Distribution of causes of death of patients with systemic lupus erythematosus (SLE) by Brazilian region between 2002 and 2011.

ICD Group	MW		NE		N		SE		S		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Musculoskeletal system and connective tissue	677	79.6	1471	77.3	629	79.7	3056	75.0	961	84.1	6794	77.5 ^a
SLE	670	98.9	1467	99.7	625	99.4	3030	99.1	953	99.2	6745	99.3 ^b
Other disorders of the musculoskeletal system and connective tissue	7	1.1	4	0.3	4	0.6	26	0.9	8	0.8	49	0.7
Circulatory system	58	6.8	99	5.2	31	3.9	281	6.9	60	5.2	529	6.0
Infectious and parasitic diseases	23	2.7	96	5.1	35	4.4	158	3.9	19	1.7	331	2.8
Respiratory system	13	1.5	38	2.0	11	1.4	112	2.7	21	1.8	195	2.2
Digestive system	16	1.9	40	2.1	16	2.0	99	2.4	17	1.5	188	2.1
Genitourinary system	17	2.0	38	2.0	19	2.4	83	2.0	6	0.5	163	1.9
Immune disorders	11	1.3	36	1.9	7	0.9	79	1.9	13	1.1	146	1.7
Endocrine, nutritional and metabolic diseases	7	0.8	34	1.8	18	2.3	62	1.5	7	0.6	128	1.5
Neoplasms	9	1.1	14	0.7	7	0.9	73	1.8	20	1.7	123	1.4
Nervous system	6	0.7	12	0.6	6	0.8	30	0.7	9	0.8	63	0.7
Musculoskeletal and connective tissue	7	0.8	4	0.2	4	0.5	26	0.6	8	0.7	49	0.6
Skin and subcutaneous tissue	4	0.5	5	0.3	7	0.9	21	0.5	3	0.3	40	0.5
Pregnancy, childbirth, and the puerperium	7	0.8	14	0.7	3	0.4	13	0.3	6	0.5	43	0.5
Congenital malformations	1	0.1	2	0.1	0	0	2	0	0	0	5	0.1
Other groups	1	0.1	1	0.1	0	0	5	0.1	0	0	5	0.1
Mental disorders	1	0.1	0	0	0	0	2	0	1	0.1	4	0
Eye, ear and mastoid process	0	0	2	0.1	0	0	0	0	0	0	2	0
Total	851	100	1902	100	789	100	4076	100	1143	100	8761	100

Source: Mortality Information System (SIM) of the IT Department of the Unified Health System – DATASUS.

MW, Midwest; NE, Northeast; N, North; SE, Southeast; S, South.

^a ICD Groups (p -value < 0.0001), Chi-square test.

^b Comparison between the regions: p -value < 0.2028, Chi-square test.

Table 4 – Distribution of the sequential causes recorded in death certificates of patients with systemic lupus erythematosus as the underlying cause of death in Brazil between 2002 and 2011.

Sequential cause	No. of records	%	No. of records/6745
Respiratory system	5081	26.4	75.3 ^a
Circulatory system	3989	20.7	59.1
Infectious and parasitic diseases	3823	19.9	56.7
Genitourinary system	2821	14.7	41.8
Immune disorders	823	4.3	12.2
Digestive system	809	4.2	12.0
Endocrine and metabolic diseases	735	3.8	10.9
Nervous system	380	2.0	5.6
Musculoskeletal system and connective tissue	233	1.2	3.5
Skin and subcutaneous tissue	226	1.2	3.4
Neoplasms	187	1.0	2.8
Mental disorders	65	0.3	1.0
Pregnancy, childbirth, and the puerperium	64	0.3	0.9
Congenital malformations	10	0.1	0.1
Eye, ear and mastoid process	7	0.0	0.1
Total	19,253	100	

Source: Mortality Information System (SIM) of the IT Department of the Unified Health System – DATASUS.

^a *p*-Value < 0.0001, Chi-square test of goodness of fit.

Table 5 – Main sequential causes of death from systemic lupus erythematosus by Brazilian region between 2002 and 2011.

ICD Group	MW	NE	N	SE	S	Total	<i>p</i> -Value ^a
Respiratory system	553	1313	608	1665 ^a	942	5081	0.0017
%	10.9	25.8	12.0	32.8	18.5	100.0	
Circulatory system	574	515	594	1385 ^a	921	3989	0.0022
%	14.4	12.9	14.9	34.7	23.1	100.0	
Infectious and parasitic diseases	653	1123 ^a	622	988	437	3823	0.0277
%	17.1	29.4	16.3	25.8	11.4	100.0	
Genitourinary system	567	598	638 ^a	528	491	2821	0.9340
%	20.1	21.2	22.6	18.7	17.4	100.0	

Source: Mortality Information System (SIM) of the IT Department of the Unified Health System – DATASUS.

MW, Midwest; NE, Northeast; N, North; SE, Southeast; S, South.

^a Comparison between the regions: Chi-square test.

system (32.8%) and the circulatory system (34.7%) in the Southeast, with statistically significant differences in relation to the other regions ($p < 0.0017$ and $p < 0.0022$, respectively). For infectious and parasitic diseases, the Northeast accounted for the highest number of records (29.4%), and this difference was statistically significant ($p < 0.0277$). In regard to diseases of the genitourinary system, there were no differences between the regions ($p = 0.9340$), although the highest proportion of cases occurred in the North (22.6%).

An evaluation of the distribution of the main sequential causes by age (Table 6) showed a decline in the proportion of diseases of the respiratory system in patients over 80 years of age, while patients between 20 and 39 years old ($p < 0.0001$) accounted for the largest share of the main groups of sequential causes. More than 60% of these groups of causes were identified in patients between 20 and 59 years of age.

Discussion

The mortality rate of SLE patients in Brazil is 4.76 deaths/100,000 inhabitants, and there is a predominance of women and whites in this group of patients. Differences between the regions are evident, with the South and Southeast states having lower mortality and the North region having higher mortality. It is worth noting the difference found in relation to a population study conducted in Norway, where mortality was a mere one death per 100,000 inhabitants.⁷

The North region had the lowest mean age at death (34.1 ± 13.7 years) of all Brazilian regions, similar to that recorded in Saudi Arabia (33 ± 18 years).⁸ On the other hand, the mean age at death in the South region was 44.7 years, in line with the 44 ± 15 years observed in a study comprising 1000 patients in seven European countries over ten years.⁹

Table 6 – Main sequential causes of death from systemic lupus erythematosus by age in Brazil between 2002 and 2011.

Sequential cause of death	Age of patient with SLE					Total
	Under 19	20–39 ^a	40–59	60–79	80 and over	
Respiratory system	454	2072	1567	779	209	5081
%	8.9	40.8	30.8	15.3	4.1	100.0
Circulatory system	197	1452	1256	712	372	3989
%	4.9	36.4	31.5	17.8	9.3	100.0
Infectious and parasitic diseases	581	1247	986	766	243	3823
%	15.2	32.6	25.8	20.0	6.4	100.0
Genitourinary system	328	1232	761	337	163	2821
%	11.6	43.7	27.0	11.9	5.8	100.0

Source: Mortality Information System (SIM) of the IT Department of the Unified Health System – DATASUS.

^a $p < 0.0001$, Chi-square test of independence.

In 2010, a study¹⁰ was published analyzing mortality in SLE patients in São Paulo state, in Brazil's Southeast region, between 1985 and 2004. According to this study, the mean age at death in this period was 35.1 ± 15.0 years, allowing us to infer that there has been an improvement in the survival of SLE patients in recent years given that the mean age at death was higher than this figure in Brazil as a whole and in the South, Southeast and Midwest regions. On the other hand, it underlines the discrepancy between Brazilian regions, given that the mean age at death from SLE in the North and Northeast regions has been lower than that in São Paulo state for more than ten years.

The number of deaths in the Northeast and Southeast regions was respectively lower and higher than expected. According to the United Nations Development Programme (UNDP),¹¹ the states with municipalities having the lowest Municipal Human Development Indices (MHDI) in the country are located the North and Northeast regions. As a result, it is necessary to be cautious when comparing mortality in the different Brazilian regions due to deficiencies in the service network currently available to the population in the North and Northeast regions. According to information provided by the IBGE,¹² the North and Northeast regions have problems related to the reporting of deaths in general, with high under-reporting rates. Under-reporting is extremely high in the Northeast (more than 26%) compared with the national average (12%) and especially with the Center-South (under 10%). This difference can explain why the number of deaths was lower than expected in the Northeast and higher than expected in the Southeast.

An analysis carried out in Morocco¹³ reported that the epidemiology of SLE in developing countries is still unknown and is probably underestimated, making it difficult to compare data with other international studies. Most Brazilian studies are restricted to the Southeast region.^{14–16}

In one of the few Brazilian studies carried out outside the Southeast region, an analysis of 63 SLE patients monitored in Paraíba state, in Brazil's Northeast region, established a relationship between poorer quality of life, measured at the beginning of the study, and a higher likelihood of death after a second analysis six years later. Of the deaths observed in that study, two were caused by systemic infection, two by

renal complications and two by SLE-related nervous system complications.¹⁷

A review published in 2014¹⁸ emphasized that SLE patients in emerging countries, such as Brazil, had a worse prognosis as a result of the low socioeconomic and educational level of these populations, in addition to delay in diagnosis, difficulties accessing health services and more frequent infections and disease complications.

SLE affects more women than men, with a ratio of 10:1.¹⁹ However, according to studies carried out in the United Kingdom,²⁰ Saudi Arabia⁸ and in the United States,²¹ as well as by multinational teams,²² mortality from SLE is higher in men. The disagreement with the findings of the present study may have been caused by the use of death records, which did not allow for the assessment of the prevalence of the disease in the population or its lethality by gender.

The main underlying cause of death observed was SLE itself, which is consistent with the findings of a European study.⁹ Diseases of the circulatory system, including all types of heart, vessel and cerebrovascular diseases, were the second most common underlying cause of death, in line with other studies.^{19,23–25}

A complex interaction of several factors, including the disease's chronic inflammatory nature, contributes to SLE being a risk factor for cardiovascular events. Inflammatory and immunological mechanisms are responsible for both the formation of atherosclerotic plaques and their instability, which may cause ruptures, thromboses and vessel occlusion, leading to ischemia and tissue infarction.²⁶ Renal involvement, which is frequently present, contributes to the development of premature coronary artery disease. Traditional risk factors, such as high blood pressure and hyperlipidemia, are common in lupus patients due to disease activity and the use of glucocorticoids.²⁷ These conditions are in addition to endothelial dysfunction and antiphospholipid antibodies, also implicated in accelerated atherosclerosis in SLE.²⁸ The overall result is high premature mortality from diseases of the circulatory system, as observed in a Finnish study in which 37% of deaths of SLE patients were attributed to cardiovascular causes.²⁹

In 2012, a study that analyzed mortality in SLE patients in São Paulo state during the period between 1985 and 2007 cited circulatory system causes of death as being

among the most important in that region, in addition to renal failure and infectious causes led by pneumonia and septicemia.¹⁵

The results regarding infectious and parasitic diseases as a cause of death in patients with SLE were in line with the results of a European study.⁹ In a Brazilian study³⁰ that evaluated 113 autopsies of SLE patients, infection was the cause of death in 58% of the cases. It is well established in the literature that infections, usually attributed to the use of immunosuppressive drugs, are a frequent cause of death in SLE patients.²² The incidence of infections in patients with SLE varies between 50 and 150 episodes for every 100 patients/year³¹; the most common sites are the respiratory, digestive and urinary tracts¹⁹; and the most frequent etiological agents are fungi, Gram-negative bacteria, and opportunistic agents, such as pneumocystis pneumonia, cytomegalovirus and members of the Herpesviridae family.³²

Disease activity was identified as an independent risk factor for infections.^{33,34} The clinical hematological manifestations of SLE, such as lymphopenia and neutropenia, as well as the treatment itself, are also risk factors for infectious diseases.³⁵ Glucocorticoids exert their anti-inflammatory and immunosuppressive effects through several mechanisms, such as interference in the functioning of leukocytes, fibroblasts and endothelial cells, as well as reduction in the number of circulating monocytes and macrophages. The intensity of these effects is proportional to the dosage and the duration of the treatment, and it is not clear if there is a threshold below which these drugs are considered safe.³⁶ Antimalarial drugs, on the other hand, reduce the occurrence of infections. Both chloroquine and hydroxychloroquine have antibacterial, antifungal and antiviral effects in addition to their known antiparasitic activity.³³

In Minas Gerais, a state in Brazil's Southeast region, a prospective observational study that analyzed 179 SLE patients during 3.3 years observed a higher frequency of deaths in this population than in the general population, especially deaths related to infections and SLE itself.¹⁶

Due to the clinical relevance of infections in SLE, it is necessary to adopt preventive measures. Vaccination is the most important of these preventive measures and should be performed in periods when the disease is stable, avoiding the BCG and live virus vaccines.³³ Although slightly weak immune responses have been observed, they are still effective.^{33,37-39}

Deaths from infection are still higher in SLE patients than in the general population; however, in recent years, there has been a decline in total SLE mortality, and this decline has been associated with a reduction in the cases of infection and renal problems,¹⁵ although the proportion of deaths with diseases of the circulatory system as a sequential cause have been increasing.²²

Patients with SLE have a higher chance of developing malignancies than does the general population.¹⁹ In a study involving 23 collaborating centers from seven countries,²² cancer accounted for more deaths than infectious diseases and was second only to cardiovascular diseases; the most frequent types were non-Hodgkin lymphoma and lung cancer. In the present study, it was not possible to evaluate the association

between SLE and malignancies due to the use of causes classified according to ICD-10 groups in the methodology.

The main causes of mortality resulting from SLE were diseases of the respiratory and circulatory systems, infectious and parasitic diseases, and diseases of the genitourinary system. These findings are similar to the results of another study¹⁵ in which the main sequential causes were related to the circulatory, respiratory, digestive and genitourinary systems and to certain infectious diseases.

According to studies carried out in the United States^{40,41} and in Tunisia,⁴² in emerging countries and ethnic minorities, SLE tends to be more severe and more symptomatic. Disease activity rates are higher, leading to accelerated damage accrual in target organs and higher mortality.

In lupus patients of Asian ethnicity evaluated in a U.S. study,⁴³ the prevalence of nephritis was high, ranging between 45% and 75%, and the mortality rate was three times higher than that of white patients.

A Moroccan study raised a question about the discrepancies in severity and mortality between minority groups and white individuals. It questioned whether the aggressive symptoms in ethnic minorities can, in fact, be explained by genetic risk factors or biological differences or whether they simply reflect the socioeconomic differences between these groups and white people.¹³

Diseases of the circulatory system and infections were more frequently mentioned in the deaths of patients over the age of 50 years.¹⁵ Respiratory system involvement can occur at some stage of the disease in more than 50% of patients, who can present pleurisy, pneumonitis, interstitial lung disease or pulmonary hypertension.⁴⁴

It is thus clear that there is a need for more effective control of the risk factors for cardiovascular diseases, both traditional risk factors and those related to SLE treatment and activity; additionally, a better understanding of the pathogenesis of atherosclerosis in this disease is needed. Infectious diseases are still very frequent, underlining the fact that there has not been appropriate control of risk factors, especially in the early stages of SLE, and that health professionals need to focus more on prevention with vaccines.

Conclusion

In Brazilian SLE patients, SLE itself was cited as the main underlying cause of death, followed by diseases of the circulatory system, infectious and parasitic diseases and diseases of the respiratory, digestive and genitourinary systems, which together accounted for the approximately 23% of the cases in which lupus was not identified as the underlying cause. There are also important differences between the studied regions, and it is important to take into consideration the under-reporting and socioeconomic differences among them.

Conflicts of interest

The authors declare no conflicts of interest.

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