Trends in systemic lupus erythematosus mortality rates in the state of São Paulo, Brazil from 1985 to 2004

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Abstract

Objectives

To estimate mortality rates and mortality trends from SLE in the state of São Paulo, Brazil.

Material and methods

The official data bank was used to study all deaths occurred from 1985 to 2004 in which SLE was mentioned as the underlying cause of death. Besides the overall mortality rate, the annual gender- and age-specific mortality rates were estimated for each calendar year by age bracket (0–19 years, 20–39 years, 40–59 years and over 60 years) and for the sub-periods 1985-1995 (first) and 1996-2004 (second), by decades. Chi-square test was used to compare the mortality rates between the two periods, as well the mortality rates according to educational level considering years of study. Pearson correlation coefficient test was used to analyse mortality trends. The crude rates were adjusted for age by the direct method, using the standard Brazilian population in 2000.

Results

A total of 2,601 deaths (90% female) attributed to SLE were analysed. The mean age at death was significantly higher in the second than in the first sub-period (36.6±15.6 years vs. 33.9±14.0 years; p<0.001). The overall adjusted mortality rate was 3.8 deaths/million habitants/year for the entire period and 3.4 deaths/million inhabitants/year for the first and 4.0 deaths/million inhabitants/year for the second sub-period (p<0.001). In each calendar year, the mortality rate was significantly lower for the better educated group. Throughout the period, there was a significant increase in mortality rates only among women over 40.

Conclusion

SLE patients living in the state of São Paulo still die at younger ages than those living in developed countries. Our data do not support the theory that there was an improvement in the SLE mortality rate in the last 20 years in the state of Sao Paulo. Socio-economic factors, such as the difficulty to get medical care and adequate treatment, may be the main factors to explain the worst prognosis for our patients.

Key words

Systemic lupus erythematosus, mortality rates, epidemiology, mortality trends

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Introduction

Various studies conducted in developed countries have shown that the survival rate of patients with SLE has increased in recent years (1-4). In the largest international multi-site cohort study, Bernatsky *et al*. (5) reported that the all-cause mortality rate declined by 60% between the 1970-1979 period and the 1990-2001 period. Similarly, a study published in 2008 confirmed the progressive decline in the all-cause mortality rate over the decades (6).

The mean age at death from SLE varies by geographic region. Age at death has been shown to correlate with the cause or causes of death (3, 7-9).

There are few studies evaluating SLE mortality rates; most of them were carried out in the 80s (1, 10-16). Studies conducted in the United States have shown that mortality rates are higher in women than in men, as well as being higher among African-Americans than among Caucasians (10, 12, 17).

Epidemiologic SLE data, such as mortality rates, are scarce in Latin America, including Brazil. This study will analyse mortality rates over the last two decades and estimate the overall mortality rate, specifically according to age and gender in the state of São Paulo, Brazil.

Materials and methods

Mortality data were obtained from the computer archives of the *Sistema Estadual de Análise de Dados* (SEADE, State System for Data Analysis), which contain information regularly extracted from death certificates related to all deaths occurring in the state of São Paulo.

The template for death certificates used in Brazil follows the World Health Organization recommendations. Death certification is compulsory and therefore there is 100% reporting coverage.

For the purposes of this study, we considered all deaths occurring between 1985 and 2004 in the state of São Paulo and in which SLE was coded as the underlying cause of death, defined as "the disease or lesion that initiated the morbid chain of events which directly caused death or the circumstances of the accident or violence that produced the fatal lesion" (18).

The family of the deceased usually provides the demographic data listed on death certificates. The causes of death stated on death certificates, as defined by the attending physician, medical resident or coroner, were later coded according to the ninth or tenth revision of the International Classification of Diseases (ICD-9 or ICD-10). From 1985 to 1995, SLE was defined as ICD-9 subcategory 710.0. Since 1996, it has been defined as ICD-10 category M32. In this study, we considered subcategories 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).The ninth and tenth revisions of the International Classification of Diseases were equalized using equivalence tables to allow the comparison of mortality rates between the periods (19, 20).

Beside the overall mortality rate, the annual gender- and age-specific mortality rates were estimated for each calendar year by age bracket (0–19 years, 20–39 years, 40–59 years and over 60 years) and for the sub-periods 1985–1995 (first sub-period) and 1996–2004 (second sub-period), by decades.

The crude rates were adjusted for age by the direct method, using the standard Brazilian population in 2000, obtained from the *Departamento de Informática do Sistema Único de Saúde* (DATASUS, Information Technology Department of the Brazilian Unified Health Care System) website (21).

Overall annual mortality rates were calculated by dividing the number of SLE deaths, per million population, for each respective year in the state of São Paulo. The mid-year populations in 1990 and 2000 were considered for the first and second sub-periods, respectively. The estimated population for each year was obtained from the Brazilian Institute of Geography and Statistics (22).

We compared the mortality rates between the two sub-periods, using the chi-square test. The mortality trends were analysed taking into consideration the entire period studied.

The mortality rates followed a normal distribution (Kolmogorov-Smirnov test), allowing the use of Pearson's correla-

tion coefficient to analyse the mortality trends throughout the period. Pearson's correlation coefficient, between time and mortality rate, was calculated for females by age bracket, and the respective regression curves were constructed. A positive correlation between these variables means a significant increase in the mortality rates over the time period.

All statistical analyses were performed using the program Statistical Package for the Social Sciences, version 13 (SPSS Inc., Chicago, IL, USA). Values of $p<0.05$ were considered significant.

We calculated the mortality rates according to educational level considering years of study from 1992 to 2004 (two groups: <8 years and ≥8 years of study). The years of study data on the general population are available just from 1992 to 2004.

The mean age at death from any cause was calculated for the state of São Paulo using data obtained from the DATASUS website (21).

Table I. Gender- and age-specific annual mortality rates for systemic lupus erythematosus, per million population, in the state of São Paulo, Brazil, 1985 to 2004.

Year	Women Age bracket, years				Men Age bracket, years			
	0–19	20–39	40–59	≥60	0–19	20–39	40–59	≥60
1985	2.1	11.3	8.2	2.8	0.0	0.8	1.3	0.0
1986	2.0	8.8	7.6	1.8	0.2	0.6	0.8	0.0
1987	2.7	8.3	7.8	1.7	0.3	1.8	1.6	1.0
1988	2.6	11.8	8.0	4.1	0.5	1.2	1.6	0.0
1989	2.0	11.4	6.7	2.4	0.2	0.6	0.8	0.0
1990	2.9	10.0	8.3	5.4	0.2	0.4	1.1	1.9
1991	3.3	10.9	10.6	7.5	0.5	1.3	1.5	0.0
1992	2.4	9.6	8.8	1.4	0.5	1.3	0.7	0.0
1993	2.3	10.7	10.6	1.4	0.5	0.5	2.1	0.9
1994	1.5	10.0	9.1	6.4	0.0	0.7	1.0	2.6
1995	2.1	8.0	6.3	4.9	0.6	1.2	2.8	0.9
1996	3.1	14.8	10.7	5.1	0.3	0.5	1.3	1.6
1997	3.2	11.0	12.0	5.0	1.1	1.0	1.8	0.0
1998	2.7	11.7	8.6	3.7	0.0	0.7	1.5	3.1
1999	2.2	10.6	13.4	7.4	0.4	1.6	0.9	3.8
2000	4.2	9.8	11.3	8.0	1.0	1.0	1.1	0.7
2001	2.5	8.0	12.4	7.4	0.3	1.9	0.8	0.7
2002	3.1	10.9	11.5	6.3	0.7	1.1	1.6	0.0
2003	3.0	9.7	10.1	9.8	0.0	0.9	1.3	1.3
2004	2.3	7.3	14.3	7.1	0.3	0.8	1.6	0.6

*Rates calculated based on data obtained from the São Paulo State System for Data Analysis and the Brazilian Institute of Geography and Statistics.

Results

In the state of São Paulo, a total of 2,601 deaths (90% female) were attributed to SLE during the 20-year period studied. Of those 2,601 deaths, 2,341 (90%) were in women. Approximately 93% of deaths were in individuals under the age of 60, and 69.2% were in individuals between the ages of 15 and 44.

The mean age at death was 35.3±15.0 for the study period as a whole and was significantly higher in the second sub-period than in the first (36.6±15.6 years *vs*. 33.9±14.0 years; $p<0.001$).

The overall annual mortality rate adjusted for age was 3.87 (standard error = 0.08, 95% CI (3.72–4.03)) per million population for the whole study period, whereas it was 3.48 (standard error = 0.10, 95% CI (3.28–3.68)) deaths per million population for the first sub-period and 4.28 (standard error = 0.11, 95% CI (4.06–4.50)] deaths per million population for the second sub-period ($p<0.001$). The relative standard errors were lower than 20.

The age- and gender-specific SLE mortality rates are shown in Table I; Figures 1 and 2 show the age-specific SLE mortality rates in each sub-period for women and men, respectively. The relative standard errors were lower than 30 for all age bracket for women, except those older than 60 years.

In women, we found that mortality rates increased rapidly until the third decade of life (in the first sub-period) and the fourth decade of life (in the second sub-period), after which they declined rapidly (in both sub-periods).

In women over 40 the mortality rates increased significantly over the study period as a whole ($r=0.735$; $p<0.001$ for the 40–59 age bracket and $r=0.729$; $p<0.001$ for ≥60 age bracket). In women under 40 no significant change was observed in the mortality rates over the study period. The relative standard errors were higher than 30 for all age bracket for men. It means that the number of male deaths was so small to analyse.

Figure 3 shows the regression curves for age-specific SLE mortality rates in women.

The mortality rates according to years

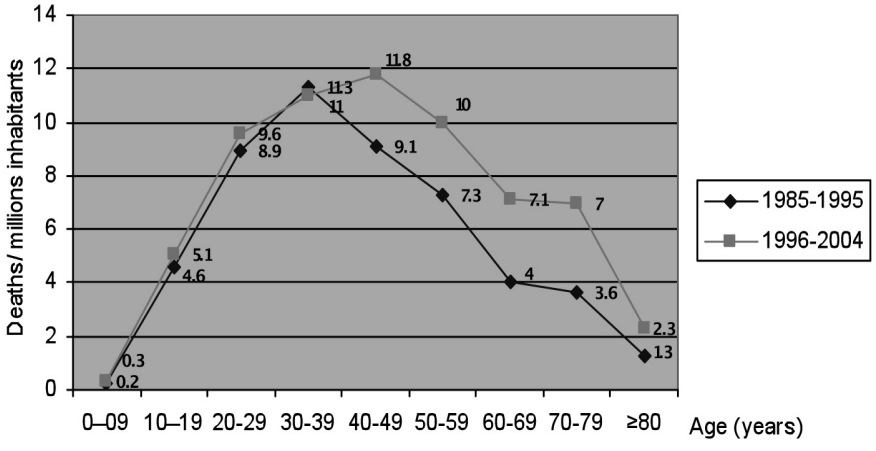

Fig. 1. Annual age-specific systemic lupus erythematosus mortality rates in women, per million population, state of São Paulo, Brazil, 1985–1995 and 1996–2004.
*Rates calculated based on data obtained from the São Paulo State System for Data Analysis and the Brazilian Institute of Geography and Statistics.

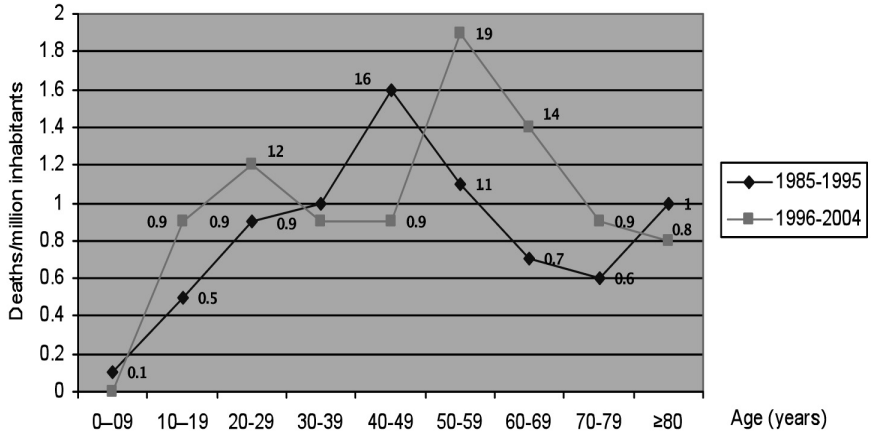

Fig. 2. Annual age-specific systemic lupus erythematosus mortality rates in men, per million population, state of São Paulo, Brazil, 1985–1995 and 1996–2004.
*Rates calculated based on data obtained from the São Paulo State System for Data Analysis and the Brazilian Institute of Geography and Statistics.

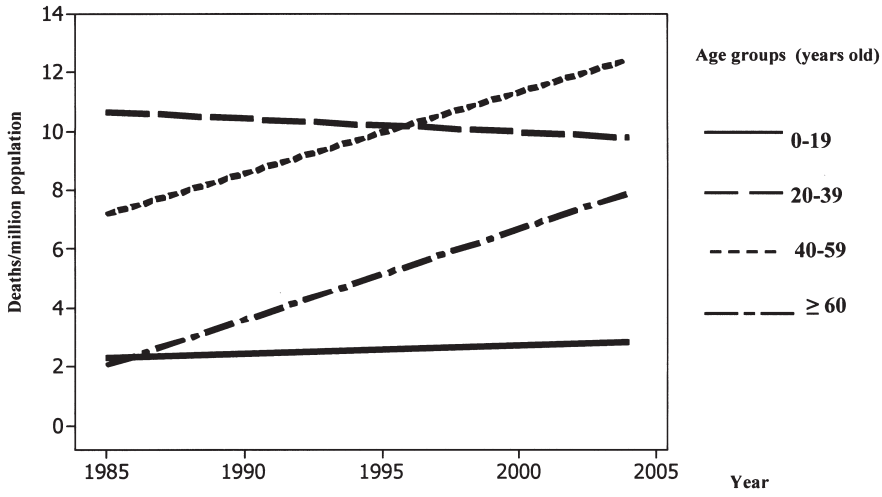

Fig. 3. Regression curves for annual age-specific systemic lupus erythematosus mortality rates in women, state of São Paulo, Brazil, 1985–2004.
*Curves obtained from the São Paulo State System for Data Analysis and the Brazilian Institute of Geography and Statistics.

of study are showed in Figure 4. There was a significant increase in the mortality rates in both groups (≥8 years and <8 years of study). In each calendar year (1992–2004), the mortality rates has ever been significantly lower for the group ≥8 years than those <8 years of study (p<0.001).

In the general population, the mean age at death from any cause in the state of São Paulo, for the study period as a whole, was 57.0±24.3 years, which was significantly higher than from SLE (p<0.001), as shown in Figure 5.

Discussion

The results of our study show that approximately 70% of the 2,601 deaths caused by SLE in the state of São Paulo during the 1985–2004 period occurred in individuals under the age of 45, indicating that SLE leads to premature death. We observed a significant increase in the mean age at death from the first to the second sub-period. Nevertheless, the mortality curves did not provide evidence to support the conclusion that there was a significant improvement in the SLE mortality rate in Brazil.

Our findings indicate that there was a marked gender difference in the mortality rates, being higher in women than in men. This finding is in accordance to those of the first mortality rate studies carried out in the United States (12, 17, 23). These findings were later corroborated by Sacks *et al*. (24), who, in 2002, conducted a study similar to ours, considering the period from 1979 to 1998 and using the Multiple Cause-of-Death Public-Use Data Files of the National Centre for Health Statistics. This higher mortality rate in women is certainly due to the greater prevalence of the disease among women.

We did not find the bimodal pattern age specific mortality among men as described by Bernatsky *et al*. (5). One possible explanation might be the smaller sample size of our study.

Despite a significant increase in the mean age at death in the second sub-period in comparison with the first, the deaths occurred at a younger age than those reported for developed countries, where the mean age at death ranges from 42 to 58.8 years (1, 9, 25-27). Our results are similar to those of a study conducted at a university hospital in the state of São Paulo (28). We emphasise that, although statistically significant, the difference between the first and second sub-periods in terms of the mean age at death might not be clinically relevant. The mean age at death from SLE in the study period as a whole was significantly lower than was the mean age at death from any cause in the general population of the state of São Paulo in the same period.

In the 2002 study conducted by Sacks *et al*. (24), 36.4% of all deaths from SLE occurred in individuals between 15 and 44 years of age. In our study, however, 69% of the SLE-related deaths occurred in individuals below the age of 45.

The fact that the age at death from SLE was lower in the state of São Paulo than in developed countries might be attributable to the earlier onset of SLE or to the greater severity of the disease in Brazil (3, 29-34). Both factors may reflect the genetic/environmental characteristics or worse socioeconomic status of the population of Latin America (35-36).

As reported in previous studies (12, 24), we observed a significant increase in the overall SLE mortality over the years, due to the increased mortality in women over 40 years of age.

The increase in the mortality rates along the period occurred independently of

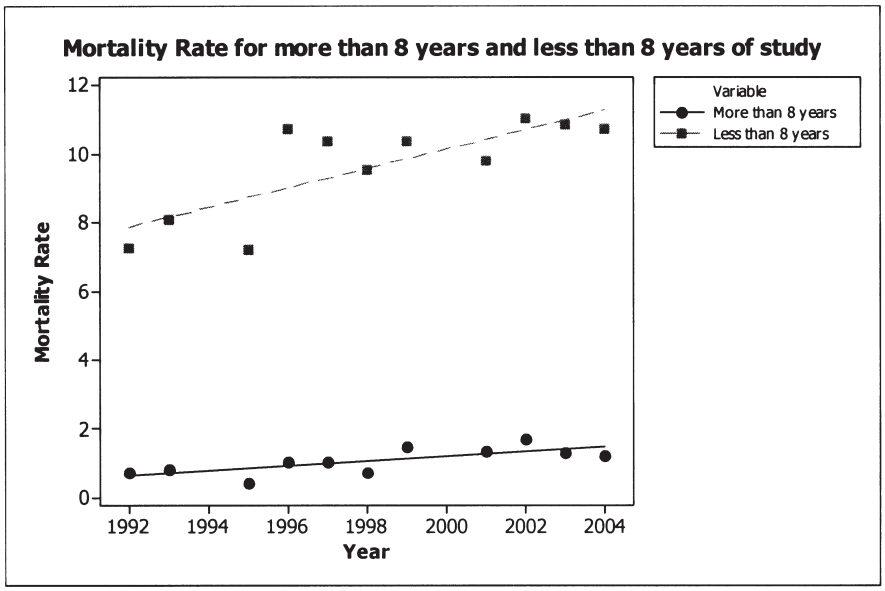

Fig. 4. Mortality rates according years of study.
*Rates calculated based on data obtained from the São Paulo State System for Data Analysis and the Brazilian Institute of Geography and Statistics.

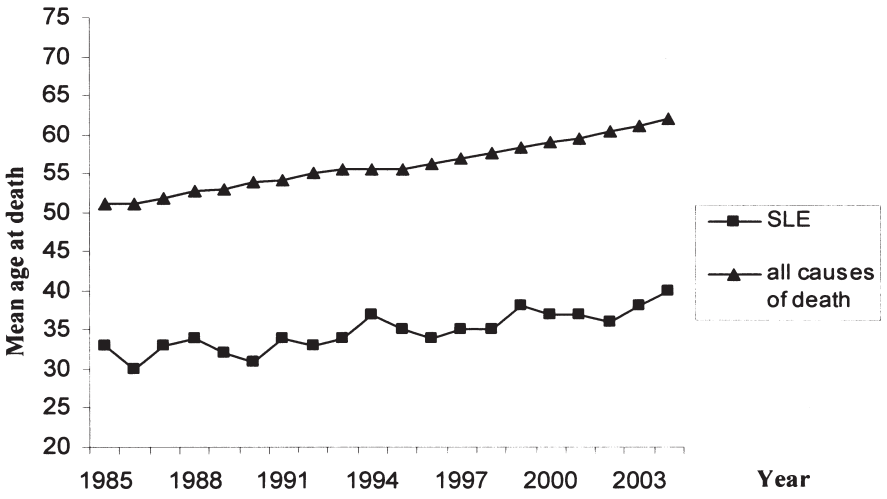

Fig. 5. Mean age at death from systemic lupus erythematosus and from all causes, state of São Paulo, Brazil, 1985–2004.
*Curves obtained from the São Paulo State System for Data Analysis and the Brazilian Institute of Geography and Statistics.

the years of study. Nevertheless, in each calendar year, the mortality rates were higher in the group less well-educated (<8 years of study), suggesting that socioeconomic factors are important to determine mortality. Beside the socioeconomic factors, it is notable that the mortality rate can vary in parallel with the prevalence, as well as the duration and severity of the disease. Demographic characteristics such as race/ethnicity, gender and age of onset are also important in determining the mortality rate (37).

One possible limitation of our study is that certain factors might have resulted in an underestimation of SLE mortality rates. Previous studies stated SLE is not always reported as the underlying cause of death in many patients with SLE (38). In addition to underreporting on death certificates, there is also the possibility that SLE is being under diagnosed.

The higher mortality rates in women over 40 might, at first glance, suggest an improvement in the survival rate of female patients with SLE. However, for this to be true, we would have also found a lower mortality rate in younger women, as described by Walsh *et al.* (39), but we did not find it.

It is very likely that the increase in overall mortality rates during the whole studied period was due to an increase in the diagnosis rate or an increase in the coding of the underlying cause of death. If so, it might be masked the decrease in mortality rates in young women and keeping the steady mortality rate. The higher mortality rate in older women might be explained by the increase in the rate of diagnosis or coding of SLE as cause of death, together with higher survival in younger women. In view of this, we would be inclined to infer an increase in the survival rate of women with SLE. However, the curve of mean age at death from SLE shows an inconsistent progression and a smaller increase than observed in the general population. These data suggest patients with SLE have received the same benefits as the general population and no specific benefits from more efficient treatment of SLE.

We can not estimate race-specific mortality rates because there is a high degree of miscegenation within the Brazilian population, particularly among Amerindians, Europeans and Africans, as demonstrated in a study of the Brazilians genomic ancestry (40).

In conclusion, we found that SLE patients in the state of São Paulo continue dying at a younger age than do those in developed countries.

We observed a significant increase in the mean age at death from SLE in more recent years, as observed in the general population; however our data do not support that there was an improvement in the SLE mortality rate in the last 20 years in the state of São Paulo. We observed that less educated individuals had worst mortality. Socioeconomic factors, such as the difficulty in obtaining medical care and appropriate treatment, together with genetic factors, might be the principal factors to explain the premature death of our patients, who might not benefit from appropriate treatment for the disease.

Further studies are needed in order to identify contributing factors to the pre-

mature death of individuals with SLE, as well as to introduce strategies and interventions that might improve the prognosis and survival of SLE patients in the state of São Paulo.

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