Mortality rates due to amyotrophic lateral sclerosis in São Paulo City from 2002 to 2006

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ABSTRACT

Objective: To describe the mortality rates of amyotrophic lateral sclerosis (ALS) in the city of São Paulo as a function of demographics, year, and region. **Method:** This was a retrospective descriptive study. Information was obtained from death certificates registered at the Program for the Improvement of Mortality Information, Municipal Health Department (PRO-AIM/SMS), coded as G12.2 according to International Classification of Diseases (ICD-10), from 2002 to 2006. **Results:** Over the studied time, were found 326 deaths (51.6% women, overall mean age of 64.1 years). Highest deaths percentages happened in those from 60 to 69 and 70 to 79 years and in white individuals. ALS mortality rates ranged 0.44/100,000 in 2002 and 0.76/100,000 in 2006. No significant changes overtime in administrative districts were found. **Conclusion:** ALS mortality rates in São Paulo were lower in comparison to other countries, however any risk factor in our environment, lifestyle or genetic characteristics were found.

Key words: mortality, amyotrophic lateral sclerosis.

Mortalidade por esclerose lateral amiotrófica no município de São Paulo de 2002 a 2006

RESUMO

Objetivo: Descrever a taxa de mortalidade da esclerose lateral amiotrófica (ELA) no município de São Paulo (MSP) de 2002 a 2006, segundo tempo, pessoa e espaço. **Método:** Estudo descritivo retrospectivo, utilizando dados das declarações de óbitos do Programa de Aprimoramento das Informações de Mortalidade (PROAIM/SMS), com G12.2 segundo Classificação Internacional de Doenças (CID 10), de 2002 a 2006. **Resultados:** Foram encontrados 326 óbitos, 51,6% mulheres, média de idade de 64,1 anos. Maiores percentuais de mortes foram encontrados nas faixas etárias de 60-69 anos e 70-79 anos e na raça branca. As taxas de mortalidade por ELA variaram de 0,44/100.000 em 2002 para 0,76/100.000 em 2006. Não houve mudanças significativas nos distritos administrativos em relação ao tempo. **Conclusão:** Taxas de mortalidade por ELA no MSP são menores, comparadas às de outros países; mas nenhum fator de risco foi encontrado no estudo em relação ao ambiente, modo de vida e características genéticas.

Palavras-Chave: mortalidade, esclerose lateral amiotrófica.

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Received 20 January 2011
Received in final form 12 August 2011
Accepted 19 August 2011

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder, causing motor neuronal death at several levels, including the motor cortex, brainstem and spinal cord. Symptoms include weakness and generalized muscular at-

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rophy leading to death[1,2]. The pathophysiology of ALS is still poorly known, and the clinical characteristics currently described remain very similar to the original description of Charcot, at the 19th century[3]. Prevalence of ALS is highest in men and in white individuals. Initial symptoms typically appear at the sixth or seventh decade of life[4].

Diagnosis is established on clinical grounds, often supported by nerve conduction studies and electromyography, neuroimaging and laboratorial tests. Diagnostic criteria were defined by El Escorial, and revised in 1998; these criteria distinguished ALS as possible, probable and definitive[5,6]. The prognosis of ALS is defined by the level of weakness, progressive muscular atrophy, dysphasia, and dysarthria due to bulbar involvement. Respiratory insufficiency due to weakness on the respiratory muscles leads to death typically from 2 to 5 years after the initial clinical manifestations[7].

Global ALS incidence ranges from 1.0 to 2.5 cases/100,000 inhabitants; prevalence ranges from 4 to 6 cases/100,000 inhabitants[8,9]. Studies suggest that mortality rates due ALS are increasing over time. In the United States, a retrospective study described rates increasing from 1.7/100,000 inhabitants in 1979, to 1.9/100,000 inhabitants in 2001[10]. Studies from other Countries also suggest this trend, raising the epidemiological interest regarding putative causes for the regional discrepancies, as well as risk factors for ALS overall[1,2,8,10].

In Brazil, the magnitude, as well as mortality rates of ALS are poorly studied. A study in Rio de Janeiro (1983) showed that mortality rates changed from 0.3/100,000 to 0.9/100,000 inhabitants[11]. In a more recent study the mortality rates showed variations from 0.2/100,000 to 0.4/100,000 in city of São Paulo[12]. This study was designed to determine the mortality statistics in estimating long term trends of ALS mortality rates in the city of São Paulo, Brazil as a function of demographics (person), time (year) and location (region) variables.

METHOD

This was a retrospective study, in which death certificates due to ALS from January of 2002 to December of 2006 happened in the city of São Paulo were analyzed. Data were obtained from The Mortality Information System (SIM), of the Program for the Improvement on Mortality Information (PRO-AIM/SMS).

Because in most cases contributory causes of death could not be obtained, only basic causes were used for calculation.

Death certificates coded as G12.2 according the International Classification of Diseases (ICD10) were included and reviewed. In addition to the code, certificates should specify ALS as the cause of death. Death certificates coded as G12.2 but with other causes of death (e.g. primary lateral sclerosis, progressive spinal amyotrophy, progressive bulbar paralysis) were excluded.

For the scope of this study we focused on the following variables: time-related variables (year of death); person-related variables (age, sex, race, marital status, job and education); region-related variables (area of living, health district, and citizenship).

At the city of São Paulo, death certificates are electronically stored by the PRO-AIM. After data collection, the database was reviewed in order to eliminate duplicated registries, as well as to revise if G12.2 corresponded to ALS. The database was then transferred to SPSS version 15® (LEAD Technologies, Inc) and statistical analyses were performed.

The descriptive analysis was carried out through comparisons of the proportions by category, together with the calculation of mean, median, and standard deviation (SD). For comparisons of categorical variables, the chi-squared test and Fisher's exact test were used. Age-specific standard mortality rates were also calculated and compared to crude mortality rates.

This study was approved by the Ethics Committees of the Federal University of São Paulo and municipal health department (313/07 - CEP/SMS). It attends the recommendation of resolution nº 196 de 10/10/96 of the Health National Council for Human Research.

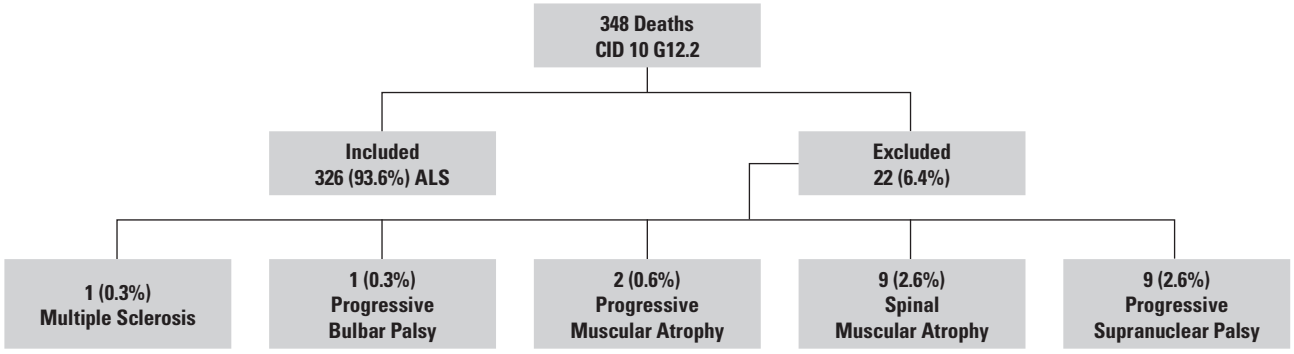
RESULTS

According to the PRO-AIM, a total of 319,729 deaths happened in the city of São Paulo from 2002 to 2006. Deaths due to ALS responded by 4.7% of deaths due to all neurological diseases (ICD 10, chapter VI), and by 88.8% of deaths due to motor neuron diseases, as displayed in Table 1.

A total of 348 death certificates were coded as G12.2, and 326 (93.6% of them) were due to ALS. Reasons for excluding death certificates are displayed in Figure.

The absolute number of death due to ALS increased as a function of year (47 in 2002, 84 in 2006), directly reflecting increased mortality rates (0.44/100,000 in 2002 and 0.76/100,000 inhabitants in 2006). A similar trend was seen for age-adjusted rates (0.44/100,000 inhabitants in 2002 and 0.78/100,000 inhabitants in 2006), as displayed in Table 2.

Regarding deaths due to ALS as a function of demographics, of the 326 cases, 168 (51.6%) were women and 158 (48.4%) were men. Mean age of death was 64.1 years (ranging from 25 to 89 years), and median was 65 years. Among men, mean age was 63.2 years; among women it was 64.9 years. For men, highest percentages of deaths happened from 70 to 79 years (52/158, 32.9%); for women, highest proportions were from 60 to 69 years



Source: PRO-AIM – SMS/SP.

Figure. Schematic representation of the assessments of deaths certificates registered in the PRO-AIM and coded as G12.2 in the city São Paulo, from 2002 to 2006.

Table 1. Total number of deaths due to neurological conditions, neuromotor disorders, and ALS, in the city of São Paulo (PRO-AIM), 2002-2006.

Year	Number of deaths	Number of deaths from chapter VI – ICD 10	Number of deaths due to neuromotor disorders	Number of deaths due to ALS	% of deaths due to ALS among neurological conditions	% of deaths due to ALS among neuromotor disorders
2002	64277	1165	54	47	4.0	87.0
2003	64909	1172	69	60	5.1	87.0
2004	65334	1364	77	66	4.8	85.7
2005	62009	1490	75	69	4.6	92.0
2006	63200	1763	92	84	4.8	91.3
Total	319729	6954	367	326	4.7	88.8

Source: PRO-AIM – SMS/SP; ALS: amyotrophic lateral sclerosis.

Table 2. Crude and adjusted mortality rates due to ALS in the city of São Paulo, from 2002 to 2006.

Year	Number of deaths due to ALS	Population	Mortality rates*	Age adjusted mortality rates*
2002	47	10600059	0.44	0.44
2003	60	10677017	0.56	0.56
2004	66	10753768	0.61	0.61
2005	69	10927985	0.63	0.64
2006	84	11016708	0.76	0.78

Source: PRO-AIM – SMS/SP; Population: IBGE; ALS: amyotrophic lateral sclerosis; *Mortality rates by 100,000 inhabitants.

(58/168, 34.6%). Differences were not statistically significantly (p>0.05), as displayed in Table 3.

The increase in the mortality percentages due to ALS happened both in men (13.9% in 2002 to 24.6% in 2006) and women (14.9% in 2002 to 26.8% in 2006). No significant differences were seen for age differences as a function of year of death (Table 3). Similar trend was seen for mortality rates. In men, rates increased from 0.44/100,000 inhabitants in 2002 to 0.74/100,000 inhabitants in 2006; in women they increased from 0.45/100,000 inhabitants in 2002, to 0.78/100,000 inhabitants in 2006.

Most deaths due to ALS happened in the white population (258/326, 79.1%), and increased rates as a function of year were seen in this group as well (38/258, 14.7% in 2002 to 65/258, 25.1% in 2006). This may just reflect the racial distribution of the city, where 63.2% of the inhabitants are white. No gender significant differences were seen within the white population (79.1% for men and 79.2% for women) (p>0.05). Furthermore, most deaths happened in married subjects (193/326, 59.2%); proportion was higher in men (114/158, 72.1%) than in women (79/168, 47.0%), as displayed in Table 3.

As for education, most ALS subjects (89/326, 27.3%), had from four to seven years of school; 65/326 (20.0%) had less than 3 years of school. A total of 56/326 (17.1%) cases were housewife or houseperson, and 54/326 (16.5%) were retired.

A total of 292/326 (89.6%) cases lived in the city of São Paulo at the time of death, while 34/326 (10.4%) were from other cities. Among those living in São Paulo, the

Table 3. Demographic factors associated to ALS in the city of São Paulo, from 2002 to 2006.

	Men		Women		Total		
Characteristics	N	%	N	%	N	%	p value
Year							
2002	22	13.9	25	14.9	47	14.4	
2003	33	20.8	27	16.1	60	18.4	
2004	32	20.2	34	20.2	66	20.2	
2005	32	20.5	37	22.0	69	21.2	
2006	39	24.6	45	26.8	84	25.8	
Total	158	100	168	100	326	100	>0.05[a]
Race							
White	125	79.1	133	79.2	258	79.1	
Black	6	3.8	6	3.6	12	3.7	
Yellow	3	1.9	2	1.2	5	1.5	
Brown	16	10.1	15	8.9	31	9.6	
Unknown	8	5.1	12	7.1	20	6.1	
Total	158	100	168	100	326	100	>0.05[b]
Marital status							
Single	12	7.6	25	14.9	37	11.3	
Married	114	72.1	79	47.0	193	59.2	
Widowed	17	10.8	46	27.4	63	19.3	
Divorced/others	10	6.3	13	7.7	23	7.1	
Unknown	5	3.2	5	3.0	10	3.1	
Total	158	100	168	100	326	100	<0.05[b]
Age (years)							
20 to 29	1	0.6	0	0	1	0.3	
30 to 39	7	4.4	2	1.2	9	2.8	
40 to 49	15	9.5	13	7.7	28	8.6	
50 to 59	35	22.2	35	20.8	70	21.5	
60 to 69	40	25.3	58	34.6	98	30.1	
70 to 79	52	32.9	48	28.6	100	30.6	
80 or more	8	5.1	12	7.1	20	6.1	
Total	158	100	168	100	326	100	>0.05[b]

Source: PRO-AIM - SMS/SP; [a]Chi-squared; [b]Fisher exact test.

highest percentages 10/292 (3.4%) lived in Parque São Lucas, and 8/292 (2.7%) lived in Jardim Paulista. No significant differences were seen for deaths due to ALS as a function of location of household.

Regarding the administrative district related with the deaths occurrence, higher number of cases happened in the districts of Vila Mariana and Bela Vista (19/326, 5.8%), Moema (15/326, 4.6%), Consolação and Parque do Carmo (14/326, 4.3%), Vila Clementino and Jardim Paulista (13/326, 4.0%), and Liberdade (10/326, 3.1%). Deaths were confirmed at 85 hospitals in São Paulo, mostly at five high complexity hospitals, referred to herein as A (26/326, 8.0%), B (19/326, 5.8%), C (14/326, 4.3%), D (11/326, 3.4%), and E (10/326, 3.1%). The number of deaths that occurred at home was 56/326 (17.2%). Finally about the birthplace, 284/326 (87.1%) of individuals were Brazilians, 19/326 (5.8%) were unknown, 10/326 (3.1%) were born in Portugal, 4/326 (1.2%) were born in Italy, 2/326 (0.6%) each were born in Spain and Japan, and 1/326 (0.3%) in the U.S., Egypt, Lithuania, Argentina and Romania. Among Brazilians 164/284 (57.7%) were born in São Paulo state, followed by Bahia and Minas Gerais (28/284, 9.9% each).

DISCUSSION

Several studies have investigated the prevalence of ALS, and better characterized samples have come from the in Europe and United States[13,14]. In Brazil few studies focused on the incidence of ALS, as well as on mortality rates associated with the disease, making it difficult to establish the magnitude and risk factors of ALS in our Country, justifying this investigation.

Besides of epidemiological studies of ALS based on the analysis of death certificate data have several limitations, mainly due to the questionable accuracy of reporting the diagnosis of ALS in death certificates, mortality statistics represent a unique source of data for epidemiological surveys over long time and on large populations.

Recent reports have suggested notable increase in mortality rates of ALS in some countries. In the United States the mortality rates increased by 50% from 1969 to 1998. Rates were similar in both genders and were higher in the elderly[15]. Increased mortality may be a consequence of increased incidence which, in turn, may reflect a particular susceptibility to risk factors, as suggested by Italian study[16]. Alternatively, it may reflect improved detection methods, increased reporting rates, better access to medical care (with increased diagnostic rates) and refinement of epidemiological methods to study ALS[17].

Our findings suggest that, similarly to what has been reported by others, ALS is rare in the Brazilian population, although being the most prevalent of the motor neuron disorders[13,14].

Regarding patient-related characteristics, we found no differences in mortality by gender. Other studies conducted in Brazil and in other Countries found that prevalence is increased in men relative to women[18-20], although more recent reports suggest a decline in the gender ratio. This apparent discrepancy may be explained by the length of our study, by certain causal factors, by subtle differences in the natural history of the disease, or by the overall lower expectancy of life of men relative to women (69.1 vs. 77.2 in the studied population)[21]. Lower expectancy of life decreases the pool of persons susceptible to develop neurodegenerative disorders of the elderly.

Peaking in age-specific incidence rates of death, as in other developed countries studies, occurred into older age-groups, with mean age at 64.1 years. Highest mortality percentages occurred from 60 to 69 years and 70 to 79 years. Considering previous national population-based series, specially a Brazilian survey done in 2000, with demonstration that mean and median ages at onset were 52 years and assuming mean survival of three years, this suggests a mean age at onset of 61 years, nine years older, in this study. Increasing age has been considered the principal individual risk for ALS. The highest incidence and mortality of ALS in the elderly may be a consequence of the populational increase in life expectance and could be a marker of better healthy assistance. Comparing with other Brazilian cities, São Paulo has one of the highest expectancy of life and has no limitation for special treatments, including high cost medications and ventilatory support.

Mortality percentages was higher in white individuals, relative to other races, likely reflecting the demography of the studied population (63.2% of individuals are white). Alternatively, the finding may reflect specific genetic predisposition. In a study focusing on ethnic variations associated with ALS, incidence was lower in black vs. white, and in those of Hispanic backgrounds[22]. Marital status and years of education are little discussed as influencing the prevalence of ALS. These variables were not associated with changes in the epidemiological pattern and likely reflected the demography of the population (most are married and received 8.4 years of formal education)[23,24].

Employment has been controversially associated with ALS, since specific work-related exposures could be risk factors. We found no association between this variable and prevalence of ALS.

Most cases were from the city of São Paulo (89.5%) and 57.7% were born in the state of São Paulo. The distribution likely reflected the demography of the population (city received 533.446 immigrants in the year of 2000). Studies have focused on the immigrant population to identify specific ALS risk factors. In London, adjusted mortality rates were lower in those from Asia, Africa and the Caribbean, relative to the British[22]. We found no association between the place of death (health district) and mortality rates, although reports were mostly issued from high complexity health centers.

In conclusion, besides of the use of official mortality statistics for descriptive epidemiological studies may have several biases, this study indicates that ALS in São Paulo city was aligned to what has been reported by international studies, although mortality rates of ALS were lower than that found in the international studies. No risk of factor was identified. The highest mortality in older people, with no difference in gender, is a special characteristic seen in developed countries.

Since ALS is likely a multifactorial disorder, prospective incidence studies are recommended as a prelude toward improving their treatment.

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