ORIGINAL ARTICLE

Amyotrophic lateral sclerosis in Belo Horizont, Brazil between 2010 and 2020: a clinical epidemiological study

Esclerose lateral amiotrófica em Belo Horizonte, Brasil entre 2010 e 2020: um estudo clínico epidemiológico

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ABSTRACT

Objective: To describe the clinical profile of individuals with Amyotrophic Lateral Sclerosis (ALS) from a reference hospital in the city of Belo Horizonte, Brazil. **Method:** This is a retrospective cross-sectional study with data collection from electronic medical records of individuals with a defined diagnosis of ALS between 2010 and 2020, in the Muscular Dystrophies reference sector of a hospital in a Brazilian capital. **Results:** A total of 103 individuals with ALS were included, with a mean age of 60±12 years, mean diagnostic age 56±12 years, and mean time of disease progression of 3±3 years. Furthermore, 70% were male, 88% with sporadic ALS, with a similar bulbar involvement between mild (32%), moderate (27%) and severe (28%), and with a higher rate of diagnosis from 50 to 70 years of age. **Conclusion:** The epidemiological data from this study are very similar to those in the literature. However, the heterogeneity of the disease, the complexity of the diagnosis and the diversity of forms that each study brings to the disease, and especially the rapid progression, make a more extensive picture difficult to be discussed. Tracing this profile is important for a more focused clinic and a more adequate management, and for that, further studies are needed.

Keywords: Amyotrophic Lateral Sclerosis, Epidemiologic Factors, Clinical Study, Brazil

RESUMO

Objetivo: Descrever o perfil clínico de indivíduos com Esclerose Lateral Amiotrófica (ELA) de um hospital de referência na cidade de Belo Horizonte, Brasil. **Métodos:** Trata-se de um estudo transversal retrospectivo com coleta de dados de prontuários eletrônicos de indivíduos com diagnóstico definido de ELA entre 2010 e 2020, no setor de referência em Distrofias Musculares de um hospital de uma capital brasileira. **Resultados:** Foram incluídos 103 indivíduos com ELA, com idade média de 60±12 anos, idade média de diagnóstico de 56±12 anos e tempo médio de evolução da doença de 3±3 anos. Além disso, 70% eram do sexo masculino, 88% com ELA esporádica, com envolvimento bulbar semelhante entre leve (32%), moderado (27%) e grave (28%), e com maior taxa de diagnóstico de 50 a 70 anos de idade. **Conclusão:** Os dados epidemiológicos deste estudo são muito semelhantes aos da literatura. No entanto, a heterogeneidade da doença, a complexidade do diagnóstico e a diversidade de formas que cada estudo traz para a doença, e principalmente a rápida progressão, dificultam a discussão de um quadro mais extenso. Traçar esse perfil é importante para uma clínica mais focada e um manejo mais adequado, e para isso são necessários mais estudos.

Palavras-chaves: Esclerose Amiotrófica Lateral, Fatores Epidemiológicos, Estudo Clínico, Brasil

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INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a degenerative pathology of the upper and lower motor neurons.[1-3] The deterioration of these neurons leads to progressive symptoms such as: muscle weakness, dysphagia, dysarthria, respiratory affections and immobility, which lead to complete dependence.[2-4] The average survival time is around 3 to 5 years after diagnosis,[5] with respiratory failure being one of the major causes of death in these patients.[4] ALS can be classified in different ways according to the onset of the first symptoms or the characteristics of the disease onset. It can be of the familial type when there is a genetic component, or sporadic when it is of idiopathic origin. About 80-90% of cases are sporadic, while 5-10% of cases are genetic with autosomal dominant inheritance.[6] ALS global incidence is 1.75 per 100,000 person-years of follow-up.[7] The incidence found is relatively low when compared to Brazil, occurring in 0.58 per 100,000 inhabitants/year,[8] with a prevalence rate of 0.9 to 1.5 per 100,000 inhabitants.[9]

Studies on the epidemiological profile and characterization of patients with ALS usually show some differences between different regions of the world.[10-13] There are some studies already published in different regions in Brazil.[8,9,14-21] However, due to the country's large territorial extension and significant socioeconomic, cultural and environmental differences, it is still difficult to draw the profile at the national level. For example, in the state where this study was conducted which has the second largest number of inhabitants in Brazil,[22] few studies have been published and with relatively small sample sizes, with a smaller coverage in the study length.[23-25] This article provides more concise data on the clinical profile and epidemiological data of these individuals than previous studies such as BMI, use of medications, surgeries, profession, exposure to alcohol and tobacco, first symptoms and stratification by age group.

The different forms of evolution and presentation of the disease make it difficult to describe it in the literature and to know the profile of these patients.[20] A survey of clinical data from these patients is important to better determine the characteristics and relevance to contribute to a more targeted clinical practice.[23]

OBJECTIVE

To describe the clinical characteristics of individuals with ALS in a reference hospital in a Brazilian capital.

METHODS

A retrospective cross-sectional study was carried out in the Muscular Dystrophies reference sector of the Julia Kubitschek Hospital, located in a large capital city in Brazil. This hospital is part of the Brazilian public health system and all ALS cases present in the public health system are referred to this service for evaluation and follow-up.

Data were collected from medical records of individuals registered in the service from 2010 to 2020 who had already died and had a definite diagnosis of ALS in its sporadic and familial forms, the classification adopted by the sector. This study was approved by the Research Ethics Committee of Hospital Júlia Kubitscheck - Fundação Hospitalar do Estado de Minas Gerais (FHEMIG).

Medical records that did not have at least 80% of the data present in the medical record and with undefined diagnoses were excluded.

Two previously trained evaluators to perform the data extraction used a standardized assessment form developed by researchers with experience in medical record data collection. A professional responsible for the sector trained the evaluators, so that they could have the most effective access and that the most recent data present in the medical chart was always collected.

The following data were collected directly from the most recent medical records using a electronic system: age (years), age at diagnosis (years), time of disease progression (years), gender, ALS classification (sporadic/familial),[26] marital status, occupation, body mass index (BMI) classification, smoking and drinking habits, gastrostomy and tracheostomy, use of medications, use of Riluzol, bulbar impairment, deambulation ability, and first symptoms. The first symptoms presented by the individuals were divided into musculoskeletal and bulbar symtoms in order to provide a better description. Nutritional status was assessed based on BMI. The classification cut-off points adopted were: underweight (BMI ≤ 18.5 kg/m²); appropriate weight (18.5 < BMI < 25 kg/m²); overweight (25 ≤ BMI < 30 kg/m²) and obesity (BMI ≥ 30 kg/m²).[27]

Descriptive statistics were used to characterize the sample, such as mean and standard deviation for each variable, as well as minimum and maximum values. In addition, percentages were used to analyze and compare the variables in terms of frequency. The chi-squared test was used to verify possible associations between categorical variables. Values of $p < 0.05$ were considered statistically significant. All analyses were performed using the statistical program SPSS for Windows version 17.0.

RESULTS

A total of 103 medical records of individuals with ALS were collected. Table 1 shows the descriptive data. Most of individuals were male (68%), had sporadic ALS (87%), with adequate weight, and a mean time of disease evolution of 3 years.

Table 1. Sample characterization (n= 103)

Characteristic	
Age (years), mean (SD)	60 (12)
Age at diagnosis (years), mean (SD)	56 (12)
Time of disease evolution (years), mean (SD)	3 (3)
Gender (male), n (%)	70 (68)
Sporadic ALS, n (%)	88 (87)
Familial ALS, n (%)	13 (13)
Marital status (married), n (%)	46 (84)
Occupation (self-employed), n (%)	26 (46)
BMI (kg/m²), mean (SD)	22 (2)

SD: Standard Deviation; ALS: Amyotrophic Lateral Sclerosis; BMI: Body Mass Index

The marital status of the individuals was distributed as: married (84%), single (6%), divorced (2%), and widowed (9%). It was observed that 46% were self-employed, 16% were retired, 27% received some salary, and 11% were housekeepers. Regarding smoking habits, 12% of the individuals were active smokers, 57% did not smoke, and 31%

had smoked at some time. The mean smoking time was 14 (± 16) years. Regarding alcoholism, the majority (83%) were non-drinkers, 9% were former drinkers, and 8% were drinkers.

Most of the individuals (60%) had already gone through some surgical procedure. Of these procedures, 42% had undergone gastrostomy and 26% tracheostomy. Regarding the use of medication, 95% of the individuals used medication, of which 73% were Riluzol. Table 2 and Figure 1 comprisescomprises the bulbar impairment. As shown, a large proportion of the individuals had some type of impairment, most of which was mild.

Table 2. Percentage of bulbar impairment distribution (n= 103)

Bulbar impairment	n (%)
No impairment	9 (13)
Mild impairment	23 (32)
Moderate impairment	19 (27)
Severe impairment	20 (28)

Most of the individuals were unable to walk (83%), and those who were able (17%), needed some type of assistive device. The most used assistive was a crutch (12%), followed by cane and walker, both with 3%. The first clinical manifestations observed by the individuals were varied. In the present study, such manifestations were distributed into musculoskeletal symptoms and bulbar symptoms.

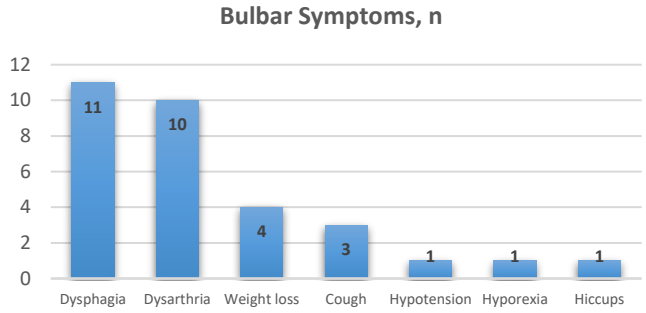

Figure 1. Bulbar symptoms (n) of the studied sample

As shown in Figure 2, the most prevalent musculoskeletal symptoms among individuals were lower limb weakness (32%), followed by upper limb weakness and falls, both with 21%. Regarding bulbar symptoms, The most prevalent symptoms were dysphagia (20%), dysarthria (19%), and weight loss (7%).

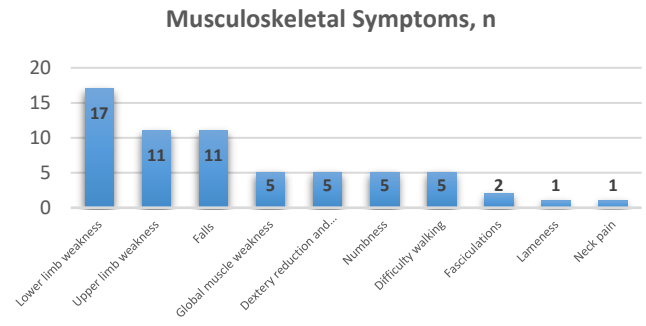

Figure 2. Musculoskeletal symptoms (n) of the studied sample

When the age of diagnosis distributed into age groups every 10 years was analyzed (Table 3), it was observed that the highest occurrence of diagnosis of individuals was between 50 to 59 years (37%), followed by 60 to 69 years (26%) and 70 to 79 years (17%), respectively. The lowest occurrence was in the 20 to 29 age group, with only one individual being diagnosed. In addition, it can be observed that the percentage is higher than 50% for males in all age groups.

Table 3. Distribution of age at diagnosis by age group and sex (n= 103)

Age group (years)	Total sample n (%)	Male n (%)
20-29	1 (1)	1 (100)
30-39	5 (5)	3 (60)
40-49	9 (9)	5 (56)
50-59	38 (37)	30 (79)
60-69	27 (26)	14 (52)
70-79	18 (17)	14 (78)
80-89	5 (5)	3 (60)

When analyzing the gender among the groups under 50 years or 50 years and older (Table 4), it was observed that there is no statistically significant difference between the age groups (chi-squared test x^2= 0.24; p= 0.41).

Regarding the type of ALS, it was observed that there is a statistically significant difference among the groups, with a higher number of cases of familial ALS in the age group under 50 years. There was a greater number of sporadic ALS cases in the group of 50 years of age or older (chi-squared test x^2= 7.57; p= 0.01).

Table 4. Sex and ALS type data according to age < 50 or ≥ 50 years (n= 103)

Variable	Age < 50 years	Age ≥ 50 years	p-value
	(n= 21; 27%)	(n= 56; 73%)	
Gender	n (%)	n (%)	
Male	13 (26)	38 (74)	0.41
Female	8 (31)	18 (69)	
Type of ALS			
Familial	5 (71)	2 (29)	0.01
Sporadic	16 (23)	54 (77)	

ALS: Amyotrophic Lateral Sclerosis; p-value: < 0.05

DISCUSSION

The present study provided comprehensive information about socio-demographic and clinical data, characteristics related to bulbar impairment, and ambulation of individuals with ALS who died between 2010 and 2020 in a reference sector for Muscular Dystrophies in a large Brazilian capital city. The findings of the present study emphasize the scarcity of data in the literature so far in relation to the distribution of individuals according to age group at the time of diagnosis.

A mean age of 60 years was found in the present study, corroborating other Brazilian studies which showed a minimum variation of 61.5 to 64.1 years,[8,17,18] in addition to an American study in which 62% of the sample was aged between 50 and 69 years.[11] The average age at diagnosis observed was 56 years, which is in line with the age range observed in a review of epidemiological studies by Longinetti, Fang[13] with a mean of 54 to 69 years, as well as in studies carried out in Brazil.[9,20,24]

The disease progression time refers to the time elapsed between diagnosis and death of the individuals. The mean

disease progression time in the present study was 3 years, which is similar to previous studies, varying from 2.5 years to 4 years.[14,19-21] These findings reflect that even though science advances, the expected life expectancy for individuals after the diagnosis is very low.

It was observed that 68% of individuals in the present study were male, which is slighltly higher when compared to other studies conducted in Italy, USA and Brazil, with values ranging between 55.4% and 63%.[11,16,20,21,24,28] The authors observed an equal percentage between men and women only in one study.[10]

These similarities and higher rates for males can be explained by the identification of females as a worse prognostic factor for ALS, as described in the literature,[29] and the greater propensity of females to have bulbar ALS at the beginning,[11] which is characterized as a worse prognosis.

Regarding the type of ALS, 13% of the individuals in the present study had ALS of the familial type, which is a higher rate for Sporadic ALS, as described in the literature.[1,6] Slightly lower values were observed in European and Brazilian studies, ranging from 3% to 5.1% for familial ALS.[10,14,16,30] Only one study demonstrated a higher rate of Sporadic ALS, with 15.2% of the individuals.[23] Slower disease progression is expected in most cases of familial ALS.[31]

The mean BMI of the individuals in this study was 22 kg/m² (adequate weight). It was demonstrated that individuals with ALS who present higher BMI have higher survival rates.[32]

Furthermore, one previous study investigated the relationship between functional levels and BMI and found that in individuals with BMI < 30, a higher BMI in the diagnosis predicts slower functional decline, which for patients with BMI > 30, a higher BMI in the diagnosis predicts faster functional decline.[33]

Due to the presence of other comorbidities and the rapid progression of ALS, 60% of the individuals in this study had already undergone some surgery; of these, 26% underwent tracheostomy and 42% underwent gastrostomy. Similar values of tracheostomy procedures (20.9%) were described, but a discrepancy in relation to gastrostomy (3.83%).[34] This can be explained by the fact that most individuals in the present study had some bulbar involvement (87%) requiring such procedures, especially in more advanced cases.

Individuals with ALS tend to use Riluzole, a drug that promotes certain benefits in patient survival[35] and is moderately effective in treating this disease.[36] In this study, 73% of the individuals were using Riluzole. The use of this drug was also observed by most individuals in studies conducted in the USA and Brazil.[11,37] The authors of the Brazilian study claim that patients treated with Riluzole had longer survival compared to those who were not treated with this drug. The high Riluzole usage rate among the individuals in the present study may also be related to the preference for this treatment option by professionals who accompany the individuals at the referral center where it was carried out.

According to Kühnlein,[38] most patients with ALS will experience bulbar symptoms at some point in their clinical course. In this study, 87% had bulbar impairment, of which the majority (32%) had mild impairment, 27% moderate and 28% severe. Different data were found by Morais,[23] where 45.2% had mild impairment, 16.1% moderate and 19.4% severe. The study by Morais[23] as far as is known, is the only one in the literature that offers descriptive data on the involvement of the bulbar with this general classification. Studies such as the one by Luchesi[39] bring a classification related to hypoventilation symptoms caused by bulbar impairment stratified into mild, moderate and severe.

A total of 83% of the individuals in the present study did not walk, the rest were dependent on assistive devices such as a crutch (12%), a cane (3%) and a walker (3%). Similar data were found in a study by Panisset.[40] However, unlike the present study, 15% were walking without assistive devices, which can be explained by the collection time of these patients, who are usually already at a more advanced stage of the disease.

Initial symptoms can vary widely, so the symptoms in the present study were divided into musculoskeletal and bulbar. It was observed that half of the individuals had limb weakness as motor symptoms, while 40% of bulbar symptoms were dysarthria and dysphagia. These data corroborate those of Raymond[11] in the USA, and by Moura in Brazil.[21] In a study conducted in 2016 in Brazil, it was found that 70% had symptoms in the spine, 19% generalized and 9.8% were bulbar.[24] The percentage of the bulbar symptoms observed in the present study were higher than those reported previously, which can be explained by the specialty of the center where the data were collected, in addition to the presence of concomitant musculoskeletal and bulbar symptoms. Herein, 63% of the entire sample received the diagnosis between 50 and 69 years, which is similar to previous studies, and showed the highest frequency of diagnoses occurring between 50-69 years of age,[20] with the highest diagnostic frequency between 50-79 years.[41,42]

It was observed that most of the diagnoses in all groups stratified by age were men, which was also evidenced by Loureiro[20] in which only the age group from 70 to 79 years old did not show a predominance of males. This data corroborates the findings related to the female gender being related to a worse prognosis of the disease.[29] We did not find statistically significant differences in terms of age when stratifying individuals younger than 50 or 50 years of age or older, which was also found by Forbes et al.[43] Regarding the type of ALS, the data obtained were similar to those of Loureiro,[20] who found a higher rate of familial ALS with patients under 50 years of age and a higher incidence of sporadic ALS aged 50 years or more.

The data from the medical records of the sample in this study belong to only one hospital center, thus limitating generalization of the findings. Despite this factor, the institution where this study was carried out is part of a reference center for muscular dystrophies, including treatment and monitoring of most individuals with ALS within the health system. Another limitation observed is the type of study, since it is not possible to establish causality between the variables. However, due to the clinical course of the disease and the low life expectancy of individuals, there is greater difficulty of designing studies with other designs.

CONCLUSION

The epidemiological data from our study are very similar to those in the literature. However, the heterogeneity of the disease, the complexity of the diagnosis and the diversity of forms that each study brings to the disease, and especially the rapid disease progression make a more extensive picture difficult to discuss.

The importance of drawing an epidemiological profile of this disabling and lethal disease is significant to improve the clinical management and to better understand the quality of life conditions of these patients. Therefore, it is necessary that more studies like this are carried out, and even in different regions, in order to obtain the particularities presented in a more objective and effective way for these patients.

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