Hospitalization and mortality from Parkinson's Disease in Brazil from 2008 to 2020

Morbidade hospitalar e mortalidade por Doença de Parkinson no Brasil de 2008 a 2020

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ABSTRACT Parkinson's Disease is irreversible and affects the central nervous system. As the disease mainly affects the elderly, attention and strategies for prevention and care for people who have the disease are essential, making it possible through the exposure of data that demonstrate the situation. The objective was to analyze the morbidity and mortality of the disease and the distribution by states and regions of Brazil from 2008 to 2020. This is an epidemiological, retrospective study, using the database of the Department of Informatics of the Unified Health System. An average of 875±166 hospitalizations per year was found, with a decrease in 2020. The most affected age group was between 60 and 79 years old, in men, but there was an increase in cases in younger people. Mortality found was 3333±759 per year, with statistically significant growth of the curve over time and higher rates in Rio Grande do Sul and Rio de Janeiro. It can be concluded that both the hospitalization rate and the mortality rate were predominant in the elderly and in males, with the South region having the highest mortality rate.

KEYWORDS Parkinson Disease. Hospitalization. Mortality. Indicators of morbidity and mortality. Brazil.

RESUMO *A Doença de Parkinson é irreversível e afeta o sistema nervoso central. Como a doença acomete principalmente idosos, é fundamental a atenção e estratégias para prevenção e cuidados para as pessoas vulneráveis à doença, através da exposição de dados que demonstrem a situação. O objetivo foi analisar a morbimortalidade da doença e a distribuição por estados e regiões do Brasil de 2008 a 2020. Trata-se de estudo epidemiológico, retrospectivo, utilizando-se o banco de dados do Departamento de Informática do Sistema Único de Saúde. Encontrou-se uma média de internações de 875±166 por ano, com queda em 2020. A faixa etária mais acometida foi entre 60 e 79 anos, em homens, mas observou-se aumento dos casos em pessoas mais jovens. A mortalidade encontrada foi de 3333±759 ao ano, com crescimento da curva ao longo do tempo estatisticamente significativa e maiores taxas no Rio Grande do Sul e Rio de Janeiro. Pode-se concluir que tanto as taxas de internamento quanto de mortalidade tiveram predomínio nos idosos e no sexo masculino, sendo a região Sul com maior taxa de mortalidade.*

PALAVRAS-CHAVE *Doença de Parkinson. Hospitalização. Mortalidade. Indicadores de morbimortalidade. Brasil.*

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Introduction

Parkinson's Disease (PD) is progressive and irreversible, it affects the central nervous system, being one of the neurological diseases that most strike individuals in the world – between 1 and 3% of the world's population over 60 years of age[1]. It was discovered in 1817 by physician James Parkinson who identified tremors in his patients. A few years later, the pathophysiology of the disease was deepened and brought to light its classic signs, such as: bradykinesia, resting tremor, rigidity and postural instability[2].

It is currently known that individuals with the disease present degeneration in the substantia nigra, with a decrease in dopamine production[3]. It has a multifactorial origin, combining genetic and environmental factors, and its diagnosis occurs through the identification of clinical symptoms and exclusion of other neurological diseases[2].

PD was considered a rare disease, however, in recent years, the number of affected individuals has increased. PD prevalence rates have grown worldwide, with a projection, for 2040, of more than 12 million individuals with PD on the planet[4]. In Brazil, notification of the disease is not mandatory; it is estimated that there are 220,000 individuals with PD[5].

As PD generally affects older adults, over 60 years of age, and considering the process of population aging, greater attention and the search for prevention and care strategies are needed for people potentially vulnerable to the disease[3,6]. The lack of compulsory notification in Brazil prevents an assertive survey of occurrences, but it is believed that there are 100 to 200 cases of the disease per 100,000 inhabitants. It is also important to emphasize that the cost of the disease directly influences the health system and, with little information on the subject, it is difficult to estimate future expenses with it[5,7]. Thus, the objective of this study was to analyze morbidity and mortality due to PD in Brazil and the distribution by states and regions from 2008 to 2020.

Material and methods

This is an epidemiological, retrospective, time-series study, using the database of the Department of Informatics of the Unified Health System (DataSUS) as a source. The period from 2008 to 2020 was defined by the availability for extracting hospitalization data in the referred system[8]. For the mortality outcome, data were obtained from the Department of Health Analysis and Surveillance of Noncommunicable Diseases – Mortality Monitoring Panel CID-10[9]. The research did not need to be submitted to the Ethics Committee, since it used a public domain database.

Individuals with PD were identified considering the variables sex, age in the year of hospitalization or death. Among the information available on the website, the following filters were inserted to search for hospital admissions: health, epidemiological and morbidity information; hospital morbidity in the Unified Health System – SUS (SUS Hospital Information System – SIH/SUS); general by place of hospitalization from 2008; geographical coverage Brazil by municipality; ICD-10 morbidity list (Parkinson's Disease); age range (30 to 80 years); gender (female-male). The following filters were used to search for deaths: year of reference; place of registration (death per occurrence); scope (unit of federation); indicator (G20 Parkinson's Disease); age group (30 to 80 years old); gender (female-male).

For the statistical analysis, numerical data were tested for normality distribution using the Kolmogorov–Smirnov test, being presented as mean and standard deviation. Qualitative variables were organized into absolute frequencies and percentages. To assess the frequencies of qualitative variables such as gender, age and place of

residence, the chi-square test was used. The hospital admission and mortality rate by region was calculated according to the 2010 Demographic Census10 ('number of hospitalizations' or 'death' divided by 'number of inhabitants', multiplied by 100,000).

Measures of association between hospital morbidity and mortality from the disease over time were calculated using Pearson's correlation (r). Statistical analyzes were performed using the software SPSS® version 22.0 and a significance level of 5% (P<0.05) was applied.

Results

Between 2008 and 2020, 11,369 people were hospitalized with PD in Brazil, with an average of 875 ± 166 hospitalizations per year, with more than 1,000 hospitalizations between 2014 and 2016 (p = 0.000), and a decrease in 2020. Mortality due to PD during the study period totaled 43,334 deaths in Brazil, with an average of 3,333 ±759 deaths per year, showing a statistically significant increase in the case curve over the years (p=0.000) (*graph 1*).

Graph 1. Hospital morbidity and overall mortality from PD between 2008 and 2020 Brazil
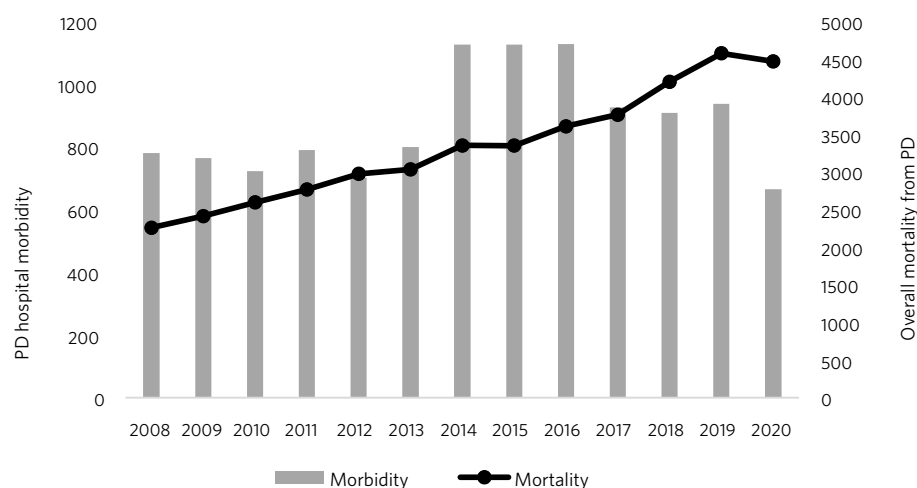
Source: DataSUS[8,9].

The age of people hospitalized with PD was predominantly in the range of 60 to 79 years old (n=6,166; 54.24%), although a significant number of hospitalizations of people under 60 years old was observed (n=3,123; 27, 47%; p=0.000). Of the total number of hospitalizations with PD during the studied period, 4,916 patients (43.24%) were female and 6,453 patients (56.76%) were male, with a statistically significant difference between frequencies (p=0.000). Only in the age group over 80 years,

most hospitalizations were female (n=1,128; 22.94%). The sum of deaths was concentrated in people over 60 years of age in both sexes (n=42,311; 97.64%; p=0.000), with emphasis on those over 80 years of age (n=24,933; 57.54 %). In all age groups, males predominated (n=23,790; 54.90%), except for those aged 80 years or more, in which females were higher (n=12,618; 64.56%) (*table 1*).

Table 1. Hospital morbidity and mortality from PD, according to age group and gender, 2008-2020, Brazil

	Hospital morbidity				Mortality			
	Feminine		Masculine		Feminine		Masculine	
Age group	n	%	n	%	n	%	n	%
30-39	102	2.07	161	2.50	1	0.01	10	0.04
40-49	350	7.12	485	7.52	52	0.27	92	0.39
50-59	697	14.18	1,328	20.58	309	1.58	559	2.35
60-69	1,158	23.56	1,778	27.55	1,363	6.97	2,541	10.68
70-79	1,481	30.13	1,749	27.10	5,201	26.61	8,273	34.78
80 or more	1,128	22.94	952	14.75	12,618	64.56	12,315	51.76
Total	4,916	100.00	6,453	100.00	19,544	100.00	23,790	100.00

Source: DataSUS[8,9].

The evaluation of hospital morbidity by Brazilian states and the Federal District, showed three states with the highest hospitalization rates between 2008 and 2020: Rio Grande do Sul (14.20/100,000), Santa Catarina (11.73/100,000) and the Federal District (10.00/100 thousand). With regard to mortality by state and Federal District, it is observed that the state of Rio Grande do Sul also had the highest mortality rate (39.87/100,000), followed by Rio de Janeiro (32.61/100,000) and Espírito Santo (31.15/100 thousand) (*table 2*).

Table 2. Hospital morbidity and mortality from PD by state and Federal District, between 2008-2020, Brazil

State	Morbidity (n)	Hospitalization Rate/ 100.000 inhabitants	Mortality (n)	Mortality Rate / 100.000 inhabitants
RS	1,519	14.20	4,264	39.87
RJ	825	5.16	5,214	32.61
ES	87	2.48	1,095	31.15
SC	733	11.73	1,683	26.93
SP	2,957	7.17	10,948	26.53
PR	880	8.43	2,698	25.83
MG	1,220	6.23	5,039	25.71
DF	257	10.00	660	25.68
MS	57	2.33	527	21.52
CE	726	8.59	1,744	20.63
GO	233	3.88	1,174	19.55
RN	53	1.67	612	19.32
SE	19	0.92	395	19.10
PB	32	0.85	690	18.32
PE	407	4.63	1,542	17.53
PI	70	2.24	516	16.55
MT	101	3.33	436	14.37
TO	50	3.61	179	12.94
BA	501	3.57	1,778	12.68

Table 2. Hospital morbidity and mortality from PD by state and Federal District, between 2008-2020, Brazil

State	Morbidity (n)	Hospitalization Rate/ 100.000 inhabitants	Mortality (n)	Mortality Rate / 100.000 inhabitants
RO	152	9.73	191	12.22
AL	9	0.29	324	10.38
PA	61	0.80	652	8.60
MA	298	4.53	564	8.58
AC	28	3.82	59	8.04
AM	79	2.27	269	7.72
RR	10	2.22	34	7.55
AP	5	0.75	47	7.02

Source: DataSUS[8,9].

When the states were grouped according to the country's regions, higher hospitalization and mortality rates were observed in the South (11.44/100,000 and 31.57/100,000) and Southeast (6.33/100,000 and 27.74 /100,000). The lowest values are found in the North region, with a hospitalization rate of 2.43/100,000 and a mortality rate of 9.02/100,000 inhabitants (*table 3*).

Table 3. Hospital morbidity and mortality due to PD, according to regions, between 2008 and 2020, Brazil

Region	Inhabitants (n)	Hospital admission 2008-2020 (n)	Hospitalization Rate/100.000 inhabitants	Mortality 2008-2020 (n)	Death rate per 100.000 inhabitants
South	27,386,891	3,132	11.44	8,645	31.57
Southeast	80,364,410	5,089	6.33	22,296	27.74
Central-West	14,058,094	648	4.61	2.797	19.9
Northeast	53,081,950	2,115	3.98	8,165	15.38
North	15,864,454	385	2.43	1,431	9.02

Source: DataSUS[8,9]; IBGE[10].

Discussion

An average of 875±166 hospitalizations per year was observed in the studied period, with a decrease in the number in 2020, probably due to the COVID-19 pandemic, in which hospital care was concentrated on cases of the disease, generating a decrease in the number of hospital admissions for other illnesses. Hospitalizations in the SUS had a 14% drop in all Brazilian regions during the pandemic period, but there is still little information in the literature on this impact on medical care in Brazil, especially in patients with chronic diseases[11]. Almeida et al.[12] state that there was a marked reduction in the number of outpatient consultations and hospitalizations in several medical areas, raising concerns about the clinical status of patients with chronic diseases who were not followed up during the period.

The age pyramid in Brazil follows the behavior observed in the rest of the world, with changes in the population profile, due to the increase in life expectancy, with repercussions on the number of people with PD[3]. The prevalence of PD with increasing age leads to

greater severity of symptoms and a higher risk of mortality from the disease[2]. In the present study, a strong association was observed between the increase in hospitalizations and mortality from PD, which may be related to the aging process that occurs in the country.

There was a significant difference in the number of hospitalizations (11,369) and mortality (43,334), which can be explained by the fact that the disease is not of compulsory notification in Brazil and is often not the main reason for hospitalization, as well as the number of hospitalizations characterizing only consultations by the SUS, registered in the SIH/SUS, and the mortality represents the national total. Macleod et al.[13] report in a meta-analysis that frail elderly people or those with comorbidities are often not referred to specialists due to suspected PD. The elderly may present the first symptoms and not report them to family members or seek care, as they associate a mild symptom with the natural aging process. It is also considered the difficulty of a more accurate diagnosis in the elderly, different from what happens in younger people, who seek services when they have the first symptoms.

Regarding deaths, Benito-Leon[14] states that deaths from PD worldwide can be underreported, given the low confidence in the diagnoses of what led to death and the disease appearing sporadically as the underlying cause in death certificates.

PD can be classified as the most common idiopathy in the world. The onset of symptoms occurs after 60 years of age and its development is related to environmental factors. There is also a subgroup of young-onset PD, linked to genetic mutations, which occurs between 21 and 40 years of age, ranging up to 50 years of age. It should be noted that in the present study, 9.66% of hospitalizations were between 30 and 50 years old. In cases of PD with early onset, it should be taken into account that this is a group of people in the productive phase, who demand specific care from the multidisciplinary team[15,16].

Regarding the age group and sex of the hospitalized individuals, there is a similarity with the systematic review carried out by Hirsch and collaborators[6], that found a predominance of people between 60 and 79 years old, a greater presence of men, with the exception of the age group of over 80 years, in which there were more cases in women. This corroborates the study of the genome of individuals from Latin American countries – including Uruguay, Brazil, Colombia, Peru and Chile – carried out by the Latin American Research Consortium on the Genetics of Parkinson's Disease (LARGE-PD), which reported that cases of PD were 53% male and had a mean age of 61.7 years and mean age of onset of 54.1 years[17]. The predominance in men can be explained due to work factors considered as risk factors for the disease, in addition to women having a neuroprotective factor, the hormone estrogen, which reduces the risk of developing PD. The influence on the development of the disease may be linked to demographic factors, such as age, sex, ethnicity, living conditions, as well as environmental factors: occupational or residential exposure to pesticides and heavy metals, being able to affect the growing number of cases over the years[2].

The fact that women with PD are the majority among people over 80 years of age can be explained by the fact that they live longer than men. Brazil is undergoing a demographic transition, with increased life expectancy and more people reaching old age[5]. According to the Brazilian Institute of Geography and Statistics (IBGE), life expectancy at birth in 2019 was 80 years for women and 73 years for men[18]. The increase in life expectancy is related to the country's social and economic development, with advances in technology and health care, improvements in basic sanitation, education and nutrition, with a relevant reduction in the number of infectious diseases[5].

Some factors such as increasing age and the presence of dementia in patients with PD are associated with increased mortality[19]. PD increases

the risk of mortality by 1.5 times and the first symptoms at a later age lead to a decrease in survival, with an average of 11 years until the individual's death[19,20]. The life expectancy of individuals diagnosed with PD is lower than that of elderly people without the disease[21].

It is important to analyze the hospitalization rates in individuals with PD, especially if the patients have already been hospitalized before, leading to a deterioration and increase in symptoms during hospitalization, which in most cases does not regress and increases the risk of mortality, since the patient has a progression of the disease after hospitalization, not returning to his previous health stage[22]. Risk factors for hospitalization such as infections, falls from standing height and fractures, lack preventive measures, considering that the management of PD is complex, through the routine of medical consultations, with the need for multidisciplinary care in order to prevent motor and non-motor complications[22-24].

The South region had the highest mortality rate from PD, 31.57/100,000 inhabitants. This region, which had an essentially agricultural economy, went through an industrialization process over the years, which was reflected in high levels of per capita income and an increase in the Human Development Index (HDI)[25,26]. Another relevant fact is that the South region has the states with the highest life expectancy in the country, such as the state of Paraná with 77.9 years, Rio Grande do Sul with 78.5 years and Santa Catarina, with the highest life expectancy in the country, of 79.9 years[18], which could explain the higher mortality rates for PD, since they mostly occur in people over 80 years of age.

The Southeast region also stands out with the second highest mortality rate, 27.74/100,000 inhabitants. This region is identified as one of the most economically developed in Brazil, with the sum of 42.5% of the Brazilian population and with one of the highest GDPs (Gross Domestic Product), being the most industrialized and populous, but which tends to have greater environments

problems and greater exposure to toxic agents that can generate PD[27]. With greater industrial growth in terms of technology and jobs, it is considered the region with the most complex sectors in the national productive structure[28].

Brazil is a country with a large territorial extension, enormous regional heterogeneity, presenting important inequalities in socioeconomic development, in the number of people, in access to health goods and services and even in life expectancy, interfering in the different patterns of aging[5], which may reflect on the regional differences found in this work.

One issue to be raised is the variation between groups with socioeconomic or ethnic differences, which affect the incidence of PD morbidity and mortality. It is believed that these differences, especially in mortality, may reflect inequalities in medical access, with more socioeconomic barriers to seeing a specialist, reducing the chance of early diagnosis of the disease[29].

This disparity in diagnosis and treatment is common in low-middle-income countries, where access to medications and forms of treatment for PD is more restricted. A comparison between European and African patients showed that the latter develop the most severe form of PD, as they take longer to start levodopa medication, which is essential for controlling the disease[30]. Latino populations, on the other hand, have contributions in their genetics from African, European and Native American ancestors, and African ancestry is significantly associated with a lower risk of PD[17].

Brazil is one of the largest consumers of pesticides in the world, with a growing sales curve over the years[31,32]. The Midwest region was the one with the highest increase in pesticide consumption (205%) in recent years. However, the Southeast and Northeast regions also had an exponential growth in the sale of the product – in 2009 there were 71,785.68 and 18,822.50 tons, respectively. In 2020, the Southeast region traded 143,665.39 tons and the Northeast region 64,086.57 tons, which may reflect in cases of PD in the future[33-35].

The manifestation of the disease may be associated with the use of pesticides, which increase the chance of degeneration of the nervous system and generate dysfunctions in the mitochondria, leading to the first symptoms of PD[36]. The use of some insecticides, herbicides and fungicides are associated with PD, such as: paraquat, glyphosate, atrazine, maneb and rotenone[37-41]. A study carried out in the south region of Brazil[42] revealed a positive association between mortality from PD and exposure to pesticides. In the western region of Paraná, research with patients with PD treated at a university hospital revealed that 74.98% of cases had been exposed to pesticides throughout their lives, corroborating a possible association between PD and exposure to pesticides[43].

The Northeast region has been expanding in the agribusiness scenario, increasing agricultural production and, consequently, the number of cases of acute intoxication and chronic effects due to exposure to pesticides. In the last decade, there was a higher lethality rate due to intoxication with pesticides for agricultural use, highlighting the importance of knowledge and control of risk factors to reduce the development rates of PD[44].

The number of men and women over 60 who died of PD has increased over time in Brazil. In the study by Rossi et al.[45], in the United States of America, there are projections for the expansion of PD, with a 56% increase in the population with PD between 2005 and 2040, which brings to light the health costs of chronic diseases, which tend to raise and impose a significant burden on the State and family members.

As a limitation of the study, it is difficult to present data of the general panorama of people hospitalized with PD in Brazil, since a portion can be attended in the private health sector that are not accounted for in hospitalizations of the SUS, as well as the under-registration due to the person being hospitalized or having died with another diagnosis.

Conclusions

It can be concluded that hospitalization rates were higher in the elderly, aged between 60 and 79 years, with a predominance of males. Regarding mortality, there was an increase in rates over the years, especially in the age group of 80 years or older, in which most deaths were men and most of them in the south region. It is also noteworthy that in the hospitalized sample there was a portion of individuals between 30 and 50 years old.

PD is an incurable disease and the number of individuals affected has been gradually increasing, reflecting the demand for health services and medications that are for continuous use, generating higher care costs for the SUS, as well as a greater probability of hospitalization.

The outcome of hospital admissions and, above all, mortality are important to contribute to public policy decision-making on neurodegenerative diseases, outlining plans for health care according to observed trends. Future case-control or cohort studies are recommended to examine causal relationships.

Collaborators

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