Neurodegenerative diseases are found mainly among the elderly population, up to 2% of those over 65 being affected globally, most commonly by Alzheimer's or Parkinson's disease, and specialist estimates indicate a doubling of the incidence every 20 years. 3.4% of the cases of dementia diagnosed in 2015 in Europe belong to Romania, 5.54% of all deaths due to this condition. From the point of view of hospitalized morbidity in the last 5 years, approximately 0.9% of all hospitalizations in Romania had as main diagnosis at hospitalization one of the neurodegenerative diseases, most commonly Alzheimer's disease or circumscribed brain atrophy, the trend of hospitalizations along years being an ascending one. Some characteristics of hospitalized morbidity in Romania would be: the fact that there are important discrepancies between different geographical areas in Romania, the differences being 10-20 times between the values observed between areas, the same being found in the case of values related to the population of each region in part; the differences between the sexes are not important, but in terms of age, over 90% of patients are people over 60; most episodes of hospitalization ended with an improvement in the patient's health, only a very small percentage resulting in the death of the person. A good knowledge of these characteristics allows the adoption of evidence based preventive and therapeutic measures that allow a better management of this chronic degenerative disease.

Keywords: Chronic diseases, neurodegenerative, Alzheimer, morbidity, hospital, Romania

INTRODUCTION

Neurodegenerative diseases, characterized by a progressive degeneration of the nervous system, are a major concern especially among the elderly population worldwide. These conditions are often associated with substantial neuronal loss, with the pattern of loss varying depending on the type of biological process. Some of these neurodegenerative diseases, such as Huntington's disease (HD) and spinocebellar ataxia, are hereditary and associated with mutations in a single gene, while other diseases of motor neurons, such as Alzheimer's disease and Parkinson's disease have an etiology, more complex, with only a percentage directly associated with the dysfunction of a specific gene. Possibly, many of these degenerative diseases have an external determinism (environmental factors) but also a form of genetic susceptibility. Both Alzheimer's and Parkinson's are diseases associated with the elderly and are becoming more common as life expectancy and the age of the population increase [1].

The most common are Alzheimer's and Parkinson's diseases, and early diagnosis and prevention of future degeneration would be the best way to treat them, as in most cases when symptoms become apparent neuronal losses are already substantial [1].

The overall prevalence of neurodegenerative diseases is around 1-2% of the global population over 65, of which about 90% are cases of Alzheimer's (1 in 300 people) and the rest include other conditions classified as neurodegenerative such as Parkinson's disease (1/5000), frontotemporal dementia (3/100000), Huntington's disease (6/1000000) etc. In terms of prevalence, the worst damage is dementia, approximately 46.8 million people worldwide had this condition in 2015, with an estimated doubling of incidents every 20 years, so that in 2030 is estimated at 74.7 million, and in 2050 131.5 million. The distribution of cases worldwide in 2015 was as follows: the European area registered 10.5 million patients, the Asian area 22.9, the American area 9.4 million, and the African area 4 million. Estimates of the increase in the incidence of dementia mainly target developing countries, if in 2015 58% of patients worldwide lived in these countries, in 2030 their percentage will reach 63%, and in 2050 68% of the global total. [2]. The regional distribution of incident cases in 2015 is as follows: 49% of the total in Asia, 25% in Europe, 18% in the Americas and 8% in Africa. The age range at which the peak of incidence appears varies regionally, so in the case of Europe and the 2 Americas the peak is between 80-89 years, in the case of Asia between 74-85 years, and in Africa between 65-74 years [2]. The economic impact of dementia alone in 2015 was $ 818 billion, and in 2018 $ 1 trillion [3]. Dementia is also considered to be the 5th leading cause of death in the world [4].

In Romania there were in 2015, 600,000 people diagnosed with dementia of different causes (Alzheimer's, senile, vascular, toxic, etc.), in 2017 there were 1,360 cases of Alzheimer's dementia per 100,000 inhabitants (1,179.61 - 1,560.26), both sexes, all ages. In Romania in 2017 there were 264484.06 prevalent cases, and in the European Union 7740480.91. Regarding deaths, also in 2017, in Romania 5.54% of all deaths were due to dementia [5]. The present study aimed to identify by using the data reported in the National DRG system the current situation, evolution in the last 5 years of reporting, on hospitalized morbidity due to neurodegenerative diseases and especially Alzheimer's disease, a disease that affects in the last decades more and more people worldwide, with younger and younger ages, inducing an increasing medical and socio-economic burden. Statistical knowledge of the situation could help the health system and societies as a whole to take effective measures for the medically, socially and financially sound management of this public health problem, especially for the elderly population.

OBJECTIVE

Identification at national, regional and local level of the geographical distribution of hospitalization episodes caused by neurodegenerative diseases, as
well as the temporal evolution of their number, in the period 2015-2019.

**Methodology**

A descriptive, retrospective study was performed, using data from the National DRG Database, data reported in continuous hospitalization by Romanian hospitals in a contractual relationship with the National Health Insurance House. In accordance with the provisions of the Order no. 1782/576/2006 on the registration and statistical reporting of patients receiving medical services in continuous hospitalization and day hospitalization, with subsequent completions and amendments, NSPHMPDB collects and processes the minimum set of patient-level data for cases treated in continuous and day hospitalization.

In this study, data reported in the period 2015-2019 were used. The aim was to analyze the data regarding the episodes of hospitalization due to neurodegenerative diseases in Romania, in the previously mentioned hospitals (hospitalizations in continuous hospitalization). The data were selected using the ICD-10-AM classification, the records were extracted and analyzed from the observation sheets which had as main diagnosis one of the codes: G30.0- Alzheimer's disease with early onset, G30.1- Alzheimer's disease with late onset, G30.8- Other forms of Alzheimer's disease, G30.9- Alzheimer's disease, unspecified, G31.0- Circumscribed cerebral atrophy, G31.1- Senile brain degeneration, not elsewhere classified, G31.2- Degeneration of the nervous system due to of alcohol, G31.8- Other specified degenerative disorders of the nervous system, unspecified, G32.0 * - Subacute combined degeneration of the spinal cord in diseases classified elsewhere, G32.8 * - Other degenerative disorders of the nervous system in diseases classified elsewhere.

In accordance with the provisions of Law 190/2018 and of Art. 13 of EU Regulation no. 679/2016, personal data are deleted at the time of transmission to NSPHMPDB, and the identification of persons for the purpose of analysis is based on encrypted CNP.

The age of the patients was calculated in years of age, as the difference between the date of hospitalization and the date of birth.

Regardless in-hospital mortality, it was assessed through an indicator constructed by reporting the number of in-hospital deaths to the total number of hospitalization episodes. The data were processed using the SQL Server Management Studio Express 2005 software, further processing and analysis was performed using SPSS and Excel. The analysis was performed according to a number of demographic and socioeconomic variables, such as the patient's gender, age, area of residence, length of stay in hospital, etc., information included in the minimum set of data reported in the DRG system by hospitals. The interpretation and presentation were done in the form of tables and graphs.

**Results**

Data processing, analysis and interpretation were performed according to a number of demographic variables and socioeconomic characteristics (sex, age, area of residence, length of stay in hospital, in-hospital mortality, discharge status) and the geographical distribution and temporal evolution of neurodegenerative diseases hospitalized in our country during 2015-2019.

1. **Total number of reported episodes of continuous hospitalization due to neurodegenerative diseases, recorded in the period 2015-2019, at national level**

In the period 2015-2019, the total number of episodes reported in continuous hospitalization for patients with a primary diagnosis of neurodegenerative diseases was 192299, representing a percentage of 0.9% of the total of 20636734 episodes of hospitalization recorded during this period. The distribution of these hospitalization episodes throughout the study period can be seen in graph no.1.

The temporal evolution of the hospitalization episodes through these diseases, in this period was an increasing one, in 2019 registering with approx. 26% more such hospitalization episodes compared to 2015, the most important increases being observed in the last 2 years. Circumscribed cerebral atrophy also increased by approx. 2.5 times the number of hospitalization episodes in 2019 compared to 2015, unlike Alzheimer's disease which recorded a slight reduction in the number of hospitalization episodes by about 15% (graph no.2).

2. **Types of neurodegenerative diseases hospitalized during this period**

Among the types of neurodegenerative diseases hospitalized during that period, the most common were Alzheimer's disease causing a percentage of 54.9% of the total nationwide and circumscribed brain atrophies (35.1%). Other hospitalized conditions of this type were: degenerative diseases of the nervous system, unspecified, other specified degenerative diseases of the nervous system, degeneration of the nervous system due to alcohol, senile degeneration of the brain, not elsewhere classified, combined subacute degeneration of the spinal cord elsewhere other specified degenerative disorders of the nervous system in diseases classified elsewhere, each with very small percentages - graph no.3.

In the category of hospitalization episodes caused by Alzheimer's disease, predominate hospitalization episodes due to Alzheimer's disease with late onset (37.4%) and Other forms of Alzheimer's disease (35.7%). Alzheimer's disease, unspecified and Alzheimer's disease with early onset have registered lower percentages (15.4%, respectively 11.4%) - graph no.4.

The evolution during the study period of these hospitalization episodes is an increasing one for all types of neurodegenerative disease, except for degenerative diseases of the nervous system, unspecified and Alzheimer's disease, the largest increase in 2019 compared to 2015 being recorded for circumscribed cerebral atrophy, an increase over 2.5 times - table no.1.

3. **Distribution of hospitalization episodes due to neurodegenerative diseases, at regional and local level, in the period 2015-2019**
The analysis of the absolute number of hospitalization episodes due to neurodegenerative diseases at regional level, in the studied period reveals that most hospitalization episodes were registered in the West and North-East regions (21.5%, respectively 17.8% of national total), compared to the regions with the fewest hospitalization episodes, South West and South-East, around 5 percent.

Depending on the development region where the patients hospitalized for Alzheimer's disease came from, the most episodes in the period 2015-2019 were registered in the South-East (23.2%) and Bucharest Ilfov (18.9%) regions, at the opposite pole being found the South West and South-East regions.

Compared to the population of the regions, in 2019 most Alzheimer's hospitalizations were registered by patients from the regions of Bucharest Ilfov (773.6 episodes/100,000 inhabitants) and the South region (768.1 episodes/100,000 inhabitants), compared to the fewest episodes in the North-East regions (248.3 episodes/100,000 inhabitants), the South-West region (283.8 episodes/100,000 inhabitants) and the South-East (285.5 episodes/100,000 inhabitants).

At the local level, most episodes of hospitalization due to neurodegenerative diseases, in absolute number were registered between 2015-2019 in Caraș Severin County and Bucharest, over 20,000 episodes, and in counties such as Brașov, Timiș, Bacău over 10,000 episodes of hospitalization. Compared to the population of each county, at the level of 2019, per 100,000 inhabitants the county where the patients with the most hospitalization episodes caused by neurodegenerative diseases come from was Caraș Severin (8306.3 episodes/100,000 inhabitants), followed by the counties of Bistrița Năsăud (2374.2 episodes/100,000 inhabitants), Bacău (1733.18 episodes/100,000 inhabitants) and Brașov (1638.3 episodes/100,000 inhabitants). The fewest hospitalization episodes were observed in Mureș, Olt and Constanța counties, below 200 episodes/100,000 inhabitants.

Regarding the distribution of hospitalization episodes caused by Alzheimer's disease at the local level, in the period 2015-2019 most such episodes were recorded in Bucharest, approx. 2.5 times more than those observed in the following leading counties in this top:
Bistrița Năsăud or Dâmbovița counties. The counties of Sălaj (73 episodes), Botoșani, Neamț, Bacău and Harghita stood out with the fewest episodes, with less than 500 episodes - graph no.9.

At the local level, depending on the population of each county, in 2019 in counties such as Bistrița Năsăud (2176.6 episodes) and Caraș Severin (1879.5 episodes) were recorded the most episodes of hospitalization/100,000 inhabitants, and others three counties had over 1000 episodes of hospitalization/100,000 inhabitants. The counties with the fewest hospitalization episodes, under 100 episodes/100,000 inhabitants were: Sălaj (29.8 episodes/100,000 inhabitants), Bacău (44.6 episodes/100,000 inhabitants), Neamț (51.9 episodes/100,000 inhabitants), Botoșani (64.4 episodes/100,000 inhabitants) and Suceava (81.7 episodes/100,000 inhabitants) - graph no.10.

4. Distribution of hospitalization episodes due to neurodegenerative diseases, according to the patient’s sex

Of the total number of hospitalization episodes due to neurodegenerative diseases at the national level, during the study period, the data analysis indicates that most belonged to females (57.5% of the total). The biggest differences between the 2 sexes are registered in the case of Bucharest Ilfov regions (27% more women), South East region (21.4% more women) or North West (18.4% more women). The most frequent episodes of hospitalization were due to circumscribed brain atrophy and Alzheimer’s disease, with women experiencing several episodes in both cases. All diseases coded as neurodegenerative except for the degeneration of the nervous system due to alcohol record an absolute number of hospitalization episodes higher in women than men - graph no.11.

The evolution of the number of hospitalization episodes during the study period was an increase in the case of both sexes, in 2019 the increase in the number of hospitalizations in continuous hospitalization being similar for both sexes, with approx. 20% compared to the initial year - graph no.11.

5. Distribution of hospitalization episodes due to neurodegenerative diseases, depending on the patient’s age

The analysis of data by age groups indicates that at national level, for the entire study period, most hospitalization episodes were recorded in the age categories over 60 years (90% of the total), as follows: group 70-79 years.
Most hospitalizations in people under 50 are due to circumscribed brain atrophy, 2% of the national total of hospitalization episodes due to neurodegenerative diseases and 6% of the national total due to circumscribed cerebral atrophy. Regarding Alzheimer's disease, the most affected were also the age groups over 60 years, especially people over 70 years, the difference between the age groups 70-79 years and over 80 years is not very large (44826 compared to 36343 hospitalization episodes), on the other hand, the difference found between the 60-69 and 70-79 age groups was almost double in absolute numbers (18391 compared to 36343 hospitalization episodes).

From the point of view of the evolution over the five years, it is found that in the age groups over 50 years there is a constant increase in the number of hospitalization episodes, the largest increases in 2019 compared to the initial year of study being observed for people over 60 years old - graph no.13.

Referring to the type of neurodegenerative disease that led to hospitalization, there is a 2.5-fold increase in the number of episodes in 2019 compared to 2015 in the case of circumscribed brain atrophy, while in the case of Alzheimer's disease the number decreased by 1.1 times. From the point of view of the distribution by regions of development of the number of hospitalization episodes in the case of people over 50 years (the most affected age categories) it is found that the most affected regions are the West (40438 episodes) and Northeast (31,156 episodes), and the least affected was the South West region (8897 episodes). The most affected counties were Caraş Severin and Bucharest (over 20,000 episodes), but also Bacău, Timiş and Brașov (over 10,000 episodes), while the least affected counties were Sălaj, Harghita and Olt (under 800 episodes).

6. Distribution of hospitalization episodes due to neurodegenerative diseases according to the average duration of hospitalization

The average duration of hospitalization for neurodegenerative diseases in continuous hospitalization was in the period 2015-2019 of 11.84 days, with a value above the average indicated being hospitalizations due to Alzheimer's disease (17.53 days average hospitalization in the case of unspecified Alzheimer's disease, an average of 16.45 days for early-onset Alzheimer's and about 15 days for late-onset Alzheimer's).
Alzheimer's and other forms of Alzheimer's disease. The rest of the diseases included in the category of neurodegenerative, recorded average duration of hospitalizations below the average of 11.84 days, circumscribed cerebral atrophy registering the lowest average duration of 6.8 days.

Evolutionarily, the average value of the length of hospitalization has seen a slight reduction in the last three years compared to 2015 and especially 2016 when the highest value was observed (13 days). The reduction in average duration was approximately 2 days for each of the last three years of the study period.

At the level of the entire study period, the hospitals with the longest average length of stay were those in the counties of Căușeni (43 days), Prahova (38.2 days) and Arad (31 days). In the hospitals from 10 of the counties, the average duration of hospitalization due to neurodegenerative diseases in the last 5 years was less than 10 days, the lowest values being observed in the hospitals from Ialomița (5.68 days), Bacău (6.71 days) or Neamț (6.73 days).

In the case of women, the average length of hospitalization was slightly longer than in the case of men (12.3 versus 11.2 in the case of men), and the elderly also recorded the average value of the longer hospital stay (over 11 days between 60 and 79 years and over 13 days for those over 80).

The category of neurodegenerative diseases with the highest average value of hospitalization was unspecified Alzheimer's disease, and the highest values were found in counties such as Neamț (76.5 days), Prahova (58.9 days), Iași (55.8 days), and the lowest values in the counties of Teleorman (3.69 days), Bistrița Năsăud (4.34 days) or Sălaj (5 days).

7. Distribution of hospitalization episodes due to neurodegenerative diseases, depending on the patient's discharge status and the share of in-hospital deaths

The analysis of the data according to the patient's discharge status indicates that out of the total number of episodes reported in continuous hospitalization due to neurodegenerative diseases, most patients were discharged in an improved condition (85.8%). 11.3% of patients were hospitalized, and less than 1% were declared cured (0.4%) or aggravated (0.7%) – graph no. 14.

The share of in-hospital mortality due to neurodegenerative diseases was for the

![Graph no. 9 Distribuția episoadelor de spitalizare datorate bolii Alzheimer, la nivel local/județean, în România, în perioada 2015-2019](image1)

![Graph no.10 Distribution of hospitalization episodes due to Alzheimer's disease at the local level, related to the population of each county, at the level of 2019](image2)
es, in the period 2015-2019 we can conclude the following:

- In Romania, in the mentioned period a percentage of 0.9% of the total episodes of hospitalization at national level was represented by hospitalizations caused by neurodegenerative diseases.
- Most of these were due to Alzheimer's disease and circumscribed brain atrophy, together representing 90% of all hospitalizations due to neurodegenerative diseases, nationwide, during this period.
- The evolutionary trend over the 5 years has been mainly in recent years an increasing one, with a quarter more hospitalizations in 2019 compared to 2015. The analysis by type of disease identified a doubling of hospitalizations in recent years in the case of atrophy circumscribed brain, however in the case of Alzheimer's disease a slight reduction was observed (15%).
- As geographical distribution, most hospitalizations due to neurodegenerative diseases were registered by patients from the West and North-East regions, around one fifth of the national total, and the least by those from the South West and South East regions, about 4 times less compared to the leading regions. Compared to the population, the best represented in terms of hospitalizations were the Bucharest-Ilfov regions, more than double the observed in the North-East, South-West or South-East.
- Locally, patients in Bucharest and Caraș Severin County are in the first 2 places in hospitalizations for neurodegenerative diseases (over 20,000 episodes), and those in Sălaj, Harghita, Olt and Tulcea are in the last places (under 1000 episodes). Compared to the population, Caraș Severin County holds the first place/100,000 inhabitants, and on the last places are Mureș, Olt and Constanța. Regarding Alzheimer's hospitalizations, Bucharest recorded 2.5 times more episodes than other leading counties such as Bistrița-Năsăud or Dâmbovița, and compared to the population, the same situation is observed, while some counties had around 2000 entire study period of 1.7%, with variations in values between 1.43 in 2017 and 1.9 in 2016. In 2019, the value increased to 1.84% from 1.77% in 2015.

Regarding Alzheimer's disease, the share of in-hospital mortality throughout the period was slightly higher, the value being 2.05%, from the category of neurodegenerative diseases being the segment with the highest share of in-hospital mortality, representing 66.2% of total deaths. by neurodegenerative diseases at national level, during the study period. The next category of neurodegenerative disease with a high share of in-hospital mortality was circumscribed brain atrophy 0.39%.

**CONCLUSIONS**

According to the analysis and interpretation of data on hospitalized morbidity from neurodegenerative diseases, in the period 2015-2019 we can conclude the following:

- In Romania, in the mentioned period a percentage of 0.9% of the total episodes of hospitalization at national level was represented by hospitalizations caused by neurodegenerative diseases.
- Most of these were due to Alzheimer's disease and circumscribed brain atrophy, together representing 90% of all hospitalizations due to neurodegenerative diseases, nationwide, during this period.
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episodes/100,000 inhabitants, others had less than 100 episodes - Sălaj, Bacău, Neamț, Botoșani and Suceava.

Most hospitalizations were suffered by women, especially in the regions of Bucharest Ilfov, South East and North West, the diseases that required hospitalization being most common in these cases circumscribed brain atrophy and Alzheimer's disease, which is also true in the case men. The evolution of hospitalizations was increasing, registering by a fifth more episodes in 2019 compared to 2015.

The most affected age groups were those over 60 years, the largest share being observed in the group 70-79 years, over a third of the total at national level. Less than a tenth of the people in the study are affected under the age of 50, the condition that most frequently led to hospitalization at this age being circumscribed brain atrophy. Alzheimer's disease predominates in the elderly.

As an average duration of hospitalization it was around 11-12 days, with a maximum average of 17.53 days in the case of unspecified Alzheimier's disease and a minimum average of 6.8 days in the case of circumscribed brain atrophy, noting a discount of about 2 days in the last 3 years. Hospitals in Covasna, Prahova and Arad counties registered the highest averages, with values two, three times higher than the national average, compared to hospitals in Ialomita, Bacău or Neamț counties with values up to 2 times lower than average hospitalizations. The gender differences were small, about a day in favor of women, the average length of hospitalization increasing with the patient's age. Alzheimer's disease recorded the highest value of the average length of hospital stay, especially in Neamț, Prahova and Iași counties, 3-4 times higher than the national level.

The vast majority were discharged in an improved state, compared to one tenth in a steady state, and very small percentages, below 1% suffered aggravations, the share of deaths related to the number of hospitalizations being below 2%, with a very slightly increased value in 2019 compared to 2015. More than half of the deaths due to neurodegenerative diseases produced during hospitalization were registered in Alzheimer's patients, on the 2nd place, at a long-distance enrolling patient with circumscribed cerebral atrophy.

The data presented, corroborated with demographic and socio-economic statistics that indicate not only an accentuated aging of the population, but also the fact that there are many elderly people with limited economic possibilities, many of them not benefiting from family support, is a challenge of today's society. The community must find the medical, financial and social resources to mobilize for the early diagnosis of such diseases, their monitoring and treatment, keeping the elderly as socially active as possible, so that a marked cognitive decline in these patients to be avoided as much as possible, in order to preserve for as long as possible the individual autonomy for the benefit of the person and the community of which he is part.

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