HEPATITES - THE FREQUENCY OF THE CONTINUOUS HOSPITALIZATION EPISODES AND THEIR SPATIAL DISTRIBUTION IN ROMANIA - ANALYSIS OF THE LAST 5 YEARS

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INTRODUCTION

Viral hepatitis is a major public health problem, both due to the nature of the consequences from the point of view of the individual health and to the burden of the disease on the health system and society in general.

Viral hepatitis occurs as a result of infection with 5 types of liver viruses: A, B, C, D and E, if infection with viruses A and E is caused by oral contamination, viruses, B, C and D are always transmitted by blood through contact with contaminated blood or fluids or sexually. Apart from "classical" liver viruses, hepatitis and other etiological agents with secondary hepatic tropism, such as herpes viruses or toxoplasma gondii, are also recognized in the determination of hepatitis. The rate of infection with virus A is a socio-economic indicator, the infection being widespread in economically poor countries where food security and access to drinking water are often a problem. In contrast to poorly developed countries where the endemcity of hepatitis A exceeds 90%, in developed countries it is below 50% of the population. In Europe, the western countries have a low prevalence, compared to the central eastern ones with an average prevalence. The trend in most countries of the European Union has been decreasing, but a geographical pattern of increasing seroprevalence is observed from north to center, south and east of the EU.

In 2017, in Romania according to the National Center for Surveillance and Control of Communicable Diseases, there were 2,512 cases of viral hepatitis A, the incidence at national level being 12.8% 000 inhabitants; 27.3% lower than in 2016.

In the case of hepatitis B and C are the cause of 1.34 million deaths worldwide annually, while about 325 million people are currently suffering from one of the two forms of hepatitis, and one in three has been exposed contact with one or both viruses. According to the data provided in June 2018 by TESSy, in 2017 in the EU countries, the crude incidence rate of hepatitis B was 6.7 cases per 100,000 inhabitants, of which 9% were reported as acute, 58% chronic, 32% unknown. The trend is downward for acute versus chronic cases, in line with global trends and reflecting the impact of national vaccination programs.

In 2017, in Romania according to the National Center for Surveillance and Control of Communicable Diseases, there were 2,512 cases of viral hepatitis A, the incidence at national level being 12.8% 000 inhabitants; 27.3% lower than in 2016.

In the case of hepatitis C, the crude incidence rate was 7.3 cases per 100,000 inhabitants in 2017, of these cases, 3% were reported as acute, 22% chronic and 75% as "unknown". In the European region there are estimated to be 14 million chronically infected with B virus, 9 million chronically infected with C virus, for non-EU countries the prevalence is 2-3 times higher. One in 50 adults is infected with hepatitis B virus or has chronic C virus infection, and over 290 million people are infected without knowing it [2]. In European countries, 45–85% of B virus infections and 20–89% of C virus infections go undiagnosed for years.

In Romania, between 2006-2018 the trend of the incidence of viral hepatitis type B was continuous and increased downwards (from 5.95 cases / 100,000 inhabitants in 2006 to 0.61 cases / 100,000 inhabitants in 2018), and for viral hepatitis C there were minor variations, from year to year, from 0.60 cases / 100,000 inhabitants in 2006 to 0.44 cases / 100,000 inhabitants in 2018.

Recognized globally as a major public health problem, viral liver infection is expected to be eliminated in the shortest possible time, and in 2016 the WHO Global Strategy on Viral Hepatitis was adopted, which includes the goal of eliminating Hepatitis B and C until 2030. At national level, through the National Health Strategy 2014–2020, 4.1. Strategic Area of Intervention 1: "PUBLIC HEALTH" Strategic Objective OS 2.5. efforts converge to reduce the incidence of priority communicable diseases: hepatitis B and C and to ensure patients' access to antiviral treatments.

Keywords: hospitalized morbidity, hepatitis, Romania
In order to reach the nationally proposed target, namely to reduce the incidence of hepatic viral infection, a fuller analysis of morbidity by this condition is required, the present study proposing an analysis of the morbidity hospitalized during the last 5 years in hospitals of the public health system from Romania.

**OBJECTIVE**

Identification at national, regional and local level of the geographical distribution of the episodes of hospitalization due to hepatitis, 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 under continuous hospitalization by the Romanian hospitals in contractual relationship with the National Health Insurance House. In accordance with the provisions of the Order. no. 1782/576/2006 regarding the registration and statistical reporting of patients receiving medical services under continuous hospitalization and day hospitalization, with subsequent completions and modifications, National School of Public Health and Professional Development Bucharest (NSPHPDB) collects and processes the minimum patient-level data set for the cases treated during continuous and day hospitalization.

In this study were used data reported for the period 2015-2019. The analysis followed the data on the episodes of hospitalization during the study period can be seen in graph no. 1.

In the period 2015-2019, at national level 20636734 hospitalization episodes recorded during continuous hospitalization due to hepatitis, recorded in the period 2015-2019, at national level

The temporal evolution of the episodes of hospitalization due to hepatitis during this period was a decreasing one, in 2019 were registered with 34% less such episodes of hospitalization compared to 2015, the most important reductions being observed at the level of years 2016 and 2019 (graph no. 2).
However, such an evolution does not necessarily suggest an absolute decrease in the number of patients with hepatitis, since a large part of the treatment or monitoring services began to be provided starting with 2015 in day hospitalization, the episodes of hospitalization in this type of hospitalization were not analyzed in this material.

2. The types of hepatitis hospitalized during this period

Of the types of hepatitis hospitalized during the period, the most frequent were viral, acute or chronic - 84.6% of the national total, chronic hepatitis caused three times the number of hospitalization episodes compared to acute ones. Alcoholic hepatitis also caused more than one tenth of the number of episodes of hospitalization in the respective period (approx. 11%), the rest of the episodes being due to other types of hepatitis such as unspecified viral ones (2.4%), autoimmune (1.1%), parasitic hepatitis (Toxoplasma) or cytomegalovirus or contact status/exposed to viral infection - graph no. 3.

In the category of hospitalization episodes determined by acute viral hepatitis, those with virus A (88.5% of total acute hepatitis) predominate, followed by hepatitis B virus (7.2%) with or without Delta agent, predominantly those without Delta agent, those caused by C virus (3.4%) and acute hepatitis E with approx. 1%.

As mentioned above, the most frequent category that determined the hospitalization during the analyzed period was the one of the chronic viral hepatitis, within it, the first one being the chronic hepatitis C (62.6% of the total episodes of hospitalization due to chronic hepatitis), followed by chronic hepatitis B (35.4%), the predominant form without Delta agent - graph no. 4.

The evolution during the study period of these episodes of hospitalization is a decreasing one for all types of hepatitis, the most marked decrease being noticed in the case of chronic viral hepatitis. In the case of the acute ones, there was a reduction in the number until 2017, registering a significant increase in 2018, so that in 2019 the number of hospitalizations will decrease again – graph no.5. It should be mentioned the same, the fact that since 2015 part of the hospitalizations of these cases has been carried out in day hospitalization, a category that has not been analyzed at this time.

3. Distribution of hospitalization episodes due to hepatitis, at regional and local level, in the period 2015-2019

At the regional level, most episodes of hospitalization due to hepatitis were recorded in the study period in the North-East regions (19% of the national total), South-
total). The West and Center regions recorded the fewest episodes of hospitalization by this main diagnosis, under one tenth each - graph no. 6.

From the point of view of the most frequent type of hepatitis encountered in the eight development regions, the first place is chronic hepatitis, followed by acute hepatitis and alcoholic hepatitis. The regions with the highest number of hospitalization episodes determined by chronic viral hepatitis were Bucharest-Ilfov, South-Muntenia and North-East - graph no. 7. In the case of acute viral hepatitis, the regions that recorded the most episodes of hospitalization during the study period were: the Center, North-East and North-West regions, and alcoholic hepatitis caused the highest number of hospitalization episodes in the North-East, South West and North West.

At the local level, most episodes of hospitalization through hepatitis were registered between 2015-2019 in Bucharest, Dolj and Iași counties, at the opposite pole being Covasna, Arad and Harghita counties, with the fewest episodes of hospitalization (graph no. 8).

The areas with the most episodes of hospitalization in the category of chronic viral hepatitis were Bucharest, Dolj, Galați, Argeș and Suceava counties, and the counties with the least such hospitalizations were Harghita, Covasna, Sălaj, Arad and Bistrița-Năsăud (under 500 episodes) (graph no. 9).

Acute hepatitis generated the most episodes of hospitalization in Mureș, Bihor, Iași and Bucharest, and the fewest in Gorj, Giurgiu and Covasna counties. Alcoholic hepatitis recorded the most admissions in Iași, Neamț and Galați counties and the fewest in Tulcea, Arad, Calarasi and Ialomița counties (under 100 episodes).

4. Distribution of hospitalization episodes due to hepatitis, by the patient's sex

From the total number of hospitalization episodes due to hepatitis at national level, during the study period, the data analysis indicates that most belonged to the female (53.5% of the total). The evolution of the number of hospitalization episodes during the study period was a decreasing one for both sexes, in 2019 the reduction of number of hospitalizations under continuous hospitalization regime was similar for both women and men, approx. with 35% for women and 32% for men - graph no. 10. Again, it should be remembered that some of the cases were solved during the day hospitalization.

From the point of view of type of hepatic impairment, for both sexes chronic and acute viral hepatitis predominated, in women almost three quarters of hospitalizations (73.6% of the total for the female sex) were due to chronic viral hepatitis and only 17.4% to acute hepatitis, while in men the proportion of hospitalization episodes due to chronic hepatitis was lower, 54.6%, and due to acute hepatitis 22.6%. For the other types of liver disease, in the case of men approx. one fifth of the hospitalizations had alcoholic hepatitis (19.4%) and almost 4 times the number of episodes of hospitalization of women compared to men was due to autoimmune hepatitis - graph no. 11.

By development regions and sexes it can be observed that women from the North-East, South-Muntenia and South-East regions had the highest number of admissions, while in men, the most affected were those from the North-East regions, South-Muntenia and Bucharest-Ilfov - graph no. 12.

At the local level it can be said that the most episodes of hospitalization were registered in case of women from Bucharest and the counties of Dolj, Galați, Suceava and Iași, and in case of men from Bucharest and the counties of Iași, Argeș, Dolj and Galați.

5. Distribution of hospitalization episodes due to hepatitis by patient's age

The analysis of the data by age groups indicates that at the national level, for the entire study period, most episodes of hospitalization were registered in the age categories 60-69 years (24% of the national total), 50-59 years (19.6%) and 70-79 years (13%). Up to 10% percentages are registered for young people under 39, as well as for the elderly, over 80 years. The percentage registered by children (age
groups 0-9 years and 10-19 years) is high, about 16%, and the percentage observed in young people up to 39 years old represents almost a quarter of the total number of hospitalization episodes (24%).

From the point of view of the evolution over five years, it is noted that in the age groups 20-29 years, 50-59 and 40-49 years, there was a significant decrease in the number of hospitalization episodes through hepatitis in 2019 compared to 2015, an increase of this number is observed only in patients over 80 years - chart no. 14.

Referring to the type of hepatitis that caused the hospitalization, in the case of children and young people the most frequent cause was acute viral hepatitis, more than one third of the cases of acute hepatitis in children 0-9 years, one third in those with ages 10 to 19 and approx. one tenth of young people up to 29 years old. For chronic hepatitis, the most frequent episodes of hospitalization were in the age groups 60-69 years (30% of the total episodes of hospitalization for chronic viral hepatitis) and 50-59 years (23%).

Regarding alcoholic hepatitis, more than half of the hospitalization episodes were between 50 and 69 years old (58%).

6. Distribution of hospitalization episodes due to hepatitis according to the average length of hospitalization

The average length of stay in the case of hospitalization episodes for hepatitis under continuous hospitalization was 6.35 days in the period 2015-2019, with a minimum around 9 days for acute viral hepatitis (the case of viral hepatitis A, without hepatic coma or acute viral hepatitis B with Delta agent, without hepatic coma) and a maximum of 13 days for acute viral hepatitis B without Delta agent, without hepatic coma. In the case of acute hepatitis C virus, the average duration was 5.39 days.

Alcoholic hepatitis required an average of 6.71 days hospitalization.

Compared to 2015, the average length of hospitalization registered an annual decrease from a value of 6.56 days to 6.46 in 2016, to 6.15 in 2017, then an increase to 6.36 in 2018, and in 2019 the value will reach 6.12 days.
The most significant reductions in the mean duration of hospitalization were observed in case of acute hepatitis B with Delta agent (coinfection) without hepatic coma (6.92 days) and acute hepatitis B without Delta agent, with hepatic coma (4.44 days). There were also increases in the average length of hospitalization, the highest being 1.69 days in case of acute hepatitis E. The highest average lengths of hospitalization for hepatitis were recorded in the hospitals in Arad and Harghita counties (11.8, respectively 11.5 days), and the lowest in Bucharest, Ialomița, Timiș, Dolj, Cluj, Giurgiu and Vrancea (between 4.15 and 5.93 days).

7. Distribution of hospitalization episodes due to hepatitis, by patient's discharge status and the hospital mortality rate

The analysis of the data according to the patient's discharge status indicates that out of the total number of episodes reported under continuous hospitalization due to hepatitis, most patients were discharged in an improved condition (89.6%). 7.3% of patients were hospitalized, 2.6% were declared as cured, and small percentages, less than 1% deceased or aggravated (0.85%) - chart no. 15.

The calculated hospital mortality rate due to hepatitis was 0.26% over the entire study period, with a slowly increasing trend from 2015, from 0.22% to 0.37% in 2019, except for the year 2017, when the lowest value of 0.17% was registered.

Most deaths were in the categories: alcoholic hepatitis, 142 hospitalization episodes ended in patient death (43% of all hepatitis deaths), chronic viral hepatitis 100 episodes (31%) and acute viral hepatitis with 46 deaths (14%). Within the two categories are distinguished for chronic viral hepatitis, those with C virus that caused the most deaths (65 out of 100), and for acute hepatitis, acute hepatitis B without Delta agent, with hepatic coma - 15 deaths.

CONCLUSIONS

In conclusion, we can say that in Romania, during 2015–2019, a percentage of less than 1% of continuous hospitalization episodes at national level was represented by the hepatitis as main diagnosis. The highest values were recorded in 2015, the values being similar in the rest of the study period. From a numerical point of view, the tendency observed in the
case of hospitalization episodes due to hepatitis was decreasing, but it must be taken into account that many cases with this main diagnosis have been solved since 2015 in day hospitalization, which may justify decrease by approx. one third of the number of hospitalization episodes in 2019 compared to 2015.

The most common type of hepatitis recorded was viral hepatitis with hepatic viruses (A, B, C, D and E), followed by alcoholic and autoimmune hepatitis, but there were other disorders due to etiological agents with secondary hepatic tropism (cytomegalovirus), parasitic hepatitis (Toxoplasma) etc.

In the category of acute viral hepatitis, the most frequent hospitalization was due to the forms of infection with virus A, the other viral types counting for approx. one tenth of the total admissions.

Of the chronic hepatitis, more than half of the episodes of hospitalization were caused by an infection with the C virus and over a third with B virus.

As with the general tendency, in the case of acute and chronic forms of viral infection with hepatitis viruses, there is a downward trend of hospitalizations over the 5 years, but as we have mentioned many cases have been probably solved through day hospitalization. Reducing the number of episodes in continuous hospitalization is more important with approx. nine percent for chronic viral hepatitis compared to acute viral hepatitis.

From the point of view of geographical distribution, it is found that the eastern and southern regions are those in which the number of hospitalization episodes is 3-4 times higher than in western regions, the highest number of hospitalization episodes being observed in these regions is caused by chronic viral hepatitis. Acute hepatitis has the highest number of hospitalizations in the northern and central regions, and the alcoholic one also in the northern regions (North-East and North-West) but also in South-West.

Locally, the counties with the highest number of episodes of hospitalization through hepatitis were in Bucharest, Dolj and Iași counties. Regarding the chronic viral hepatitis the most important impact is found in Bucharest, Dolj, Galați, Argeș and Suceava, and in case of acute viral hepatitis in counties of Mures, Bihor, Iași and Bucharest. Alcoholic hepatitis recorded the most admissions in counties from Moldova: Iași, Neamț and Galați.

The analysis of distribution of cases according to the gender of patient indicates a higher proportion of the women admitted, while the decreasing evolution in the number of hospitalization episodes is similar for both genders. From the point of view of the type of viral disease, both sexes were predominantly hospitalized for the treatment of chronic viral hepatitis, in the case of women the number of hospitalization episodes for this type of disease was greater by approx. one fifth compared to men. Another important cause of hospitalization in men was alcoholic hepatitis, accounting for about one fifth of the total number of hospitalizations of this kind.

Graph no. 11. Distribution of the number of hospitalization episodes by type of hepatitis and the patient's gender, in Romania, between 2015-2019

Graph no. 13. Distribution of the number of hospitalization episodes due to hepatitis by age groups of patients, in Romania, in the period 2015-2019
Graph no. 12. Distribution of number of hospitalization episodes due to hepatitis by development regions and patient’s gender, in Romania, between 2015-2019

Graph no. 14. Evolution of the number of hospitalization episodes due to hepatitis, by age groups of the patients, in Romania, in 2019 compared to 2015
As a geographical distribution of the hospitalizations by gender, the women with the highest number of admissions came from the counties of south-western regions (Dolj), Moldova (Galati, Suceava, Iasi counties) and Bucharest, and the men from the counties of Moldova (Iasi, Galati), but also from the upper regions, south-western, Dolj, Arges and Bucharest.

Over half of the hospitalization episodes through hepatitis have been registered in the age categories over 50 years, but their tendency in the last 5 years has been decreasing. From the point of view of the type of hepatitis, the young people and children register hospitalization through acute viral hepatitis, but adults were admitted mostly because of chronic viral hepatitis. Alcoholic hepatitis mainly affects people between ages of 50 and 69.

The average duration of hospitalization for this type of disease, at national level, was 6.35 days, with higher values, double, for acute viral hepatitis C or B virus (around 12-13 days) or lower average in the case of chronic hepatitis (5.39 days in the case of chronic hepatitis C virus). For alcoholic hepatitis, an average hospitalization was slightly above the national average.

The average value for the duration of such hospitalization registered a slight decrease from 2015 compared to 2019, the reduction being mainly achieved by reducing the duration of hospitalization episodes, especially in the case of acute viral hepatitis (with B virus with or without Delta coinfection). In the hospitals in the western and central regions (Arad and Harghita counties) the highest average lengths of hospitalization were recorded, almost double the national average of the study period.

The vast majority of the hospitalization episodes were completed with patients declared to be improved and only a small percentage died or their condition worsened. In the category of deaths, patients were admitted for alcoholic hepatitis or those with chronic viral hepatitis, among whom those infected with the C virus predominated.

We consider that a more in-depth analysis, including data that is not part of the minimum data set available in this database, but also the inclusion of data on day hospitalization would be necessary in the future in order to outline a real picture of what is affecting the romanian population, in order to improve its health, as well as to improve the medical services provided to patients, in accordance with their needs and the current resources of the health system.

Graph no. 15 The number of episodes of hospitalization due to hepatitis by state of patient’s discharge, in Romania, between 2015-2019

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