THE MOST FREQUENT HOSPITALIZATION EPISODES IN CHILDREN WITH TUMORS, IN ROMANIA, IN THE LAST 5 YEARS

**BACKGROUND**

Every year, around 300,000 children aged 0-19 years are diagnosed with cancer in the world, this disease being the main cause of non-accidental death in children and adolescents in developed countries and in an increasing number of developing countries [1], [2]. If in countries with high income/per capita 80% of treated children can be cured, in countries with average or small income/per capita, with insufficient medical and financial resources and limited access to health services this percentage is reduced to 20% [1] or even 10% [2], although the largest number of children (8 out of 10) diagnosed with cancer is found in these countries [3]. The annual incidence rate varies between 50 and 200/million in children under 15 and between 90 and 300/million in children over 15, but data are unavailable in many underdeveloped countries, with statistics only for about a fifth of the global population. [4].

A recent (2016) report by the International Agency for Cancer Research (IARC) estimates about 80000 deaths/annually determined by this condition globally [2].

The most common neoplasms in children are blood cancers - leukemias or lymphomas (almost half), cerebral cancers and embryonic tumors (retino, nephro, or neuroblastoma) [1] [2] [4]. Central nervous system tumors are placed on second place with 20% of cases, lymphomas are about 12%, and in children up to 5 years embryonic tumors represent one-third of the total at this age [5]. Among adolescents (15-19 years), the annual incidence rate was between 2001-2010 of approx. 185/million adolescents, the most common being lymphomas (23%) and carcinomas or melanoma (21%) [5].

In Romania, according to the analysis of the National Cancer Registry, the incidence of the disease at these ages remained relatively constant from year to year, between 2010-2015, the mean value was 9.86/100.000 people aged between 0 and 19, annually 400 children are diagnosed with cancer, and one third of the total were under 4 years of age. In our country as well as in all over the world predominates leukemias (31%) and lymphomas (15%), followed by tumors of the central or peripheral nervous system (20%) and tumors of the bones and soft parts 1 of 6) [6].

The complexity and severity of neoplastic disease determines the need for frequent hospitalizations of these patients not only for the purpose of diagnosis but also for the establishment and follow-up of the therapeutic course so that an analysis of the situation in terms of admission frequency research is required.

With the National DRG database, the National School of Public Health, Management and Professional Development has conducted an analysis of the situation of continuous hospitalization of children who have been diagnosed with this condition and treated in public hospitals in Romania in the last 5 years, the results being presented below.

**O B J E C T I V E**

Identification at national, regional and local level of the geographical distribution of hospitalization episodes due to the main three classes / categories of tumors that most frequently caused hospitalization in children (0-18 years) and the evolution of their number during 2013-2017.

**M E T H O D O L O G Y**

The data analysis from the National DRG Database was descriptive, retrospective using, data reported under continuous hospitalization by the Romanian hospitals, which are in contractual relation with the National Health Insurance House. According to the law, the data are also reported monthly to the National School of Public Health, Management and Professional Development Bucharest.

The analysis of the data regarding hospitalization episodes in children in Romania, in the mentioned hospitals (episodes of hospitalization in continuous hospitalization) targeted the period 2013-2017. The data were selected using the ICD-10-AM classification, the records for the Tumors diagnostic class were extracted and analyzed, based on the diagnosis name and the diagnostic subclass name. The diagnostic subclass included the following most frequent tumors that required hospitalization (established by a previous study): malignant tumors of the lymphoid, hematopoietic and related tissues (C81-

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C96), malignant tumors of the eye, brain and other parts of the nervous system central (C69-C72) and tumors with unpredictable evolution or unknown behavior (D37-D48).

Episodes of hospitalization for patients aged 18 years and below were studied.

The data was processed using the SQL Server Management Studio Express 2005 software, further processing and analysis was performed using SPSS and Excel programmes. The analysis was based on a series of demographic and socio-economic variables such as the patient's gender, age, residence, length of hospitalization, etc., information included in the minimum data set reported in DRG by hospitals. Interpretation and presentation was done in the form of tables and graphs.

RESULTS

Interpretation of the results was performed in relation to the demographic and socio-economic variables available through the minimum set of data from the National DRG database (gender, age, residence environment, length of hospitalization, in-hospital mortality rate, discharge status, discharge type) following geographical distribution and temporal evolution of hospitalizations due to the main types of tumors diagnosed in children in hospitals in Romania during 2013-2017.

1. The most common malignant tumor diagnostics in children aged 0-18 years, requiring hospitalization between 2013 and 2017, at national level

In the analyzed period, were registered a total of 28,762 hospitalization episodes due to the most common types of malignant tumors (malignant tumors of the lymphoid, hematopoietic and related tissues (C81-C96), malignant tumor of the eye, brain and other parts of the central nervous system (C69-C72), and tumors with unpredictable evolution or unknown behavior (D37-D48). Most frequently, in the period 2013-2017, were hospitalized children with malignant tumors of lymphoid, hematopoietic and related cases - 17,489 episodes (60.8% of the most common malignancies in children), but also children with malignant tumors of the eye, brain and other parts of the central nervous system - 5840 episodes (20.3%) or those with unpredictable tumors or unknown behavior - 5433 episodes (18.9%) - graph no.1.

From year-to-year distribution, there is a steady decrease in each year of the study period up to 2016, with about 20% of all hospitalization episodes annually occurring through these types of tumors. A somewhat higher figure was seen in 2013 and 2014, after which there was a reduction in the number in 2015 and 2016, so that in 2017 a new growth took place - graph 2. A similar evolution can be seen in malignant tumors of lymphoid, haematopoietic and related tissue, and partly in the case of malignant tumors of the eye, brain and other parts of the central nervous system, but in the case of unpredictable tumors or unknown behavior, the number of hospitalization episodes has increased over the last years of the study period as compared to 2013.

2. Types of tumors that caused hospitalization of children 0-18 years, during 2013-2017

The most common type of tumor that caused hospitalization, as can be seen in graph no. 3, was acute lymphoblastic leukemia in remission, 20% of the total period, or lymphoblastic leukemia with absence of remission specification - 17% - graph no.3. This type is followed by malignant tumor of cerebellum and Hodgkin's disease. The graph below highlights the types of malignancies that most commonly occurred in the children's admission in hospital during the study period. Thus, besides hematopoietic and lymphoid system malignancies (lymphoblastic leukemias, myeloids, Hodgkin's lymphomas and non-Hodgkin's lymphomas, connective tissue tumors) also occurred cerebral tumors (cerebellum, brainstem, supra or infratentorial, ventricular tumors), retinal malignancies or other tumors with unpredictable or unknown development.

Over the study period, a reduction in the number of hospitalizations for a series of tumors (eg, lymphoblastic leukemia, Hodgkin's disease, cerebellar tumors or brainstem, Burkitt tumor, etc.) was observed, so that the number of admissions episodes in 2017 was lower than in 2013, with the largest reduction seen for Burkitt's non-Hodgkin's diffuse lymphoma or acute lymphoblastic leukemia, without mentioning remission. Other types of tumors determined a higher number of hospitalization episodes in 2017 compared to 2013, eg ovarian tumor with unpredictable and
unknown evolution, brain tumors, supra or infratentorial with unpredictable and unknown evolution (with doubling of the number of cases in 2017), retinal tumor, malignant brain cerebral ventricle, connective tissue tumor, and other soft tissues with unpredictable and unknown evolution - table no1.

3. Distribution of hospitalization episodes due to tumors in children, at regional and local level, during 2013-2017

According to the data analysis, with the exception of the South Region where the highest number of hospitalizations (16% of the total national) and West Region were observed with almost half of the number of episodes registered in the South, the rest of the development regions recorded close proximity around 12-13% of the national total - graph no. 4.

The overall trend in development regions was downward, with a decrease of about 15%, from 6309 episodes registered in 2013 to 5403 admissions in 2017. Except for two regions, West a 22% increase) and the Center, for all the rest, this downward trend is preserved, even though there have been some variations in the sense of increases over the years - table no. 2. The most significant decrease was observed for North West (about 35%) and South (about 25%).

In five of the eight development regions, the Center, North-East, North-west, South-East and South-West regions predominated malignant tumors of lymphoid, haematopoietic and related tissue, and malignant tumors of the eye, brain, and other parts of the system central nervous system, but in the Bucharest-Ilfov, West and South regions outside the malignant tumors of lymphoid, hematopoietic and related tissues, more frequent were tumors with unpredictable evolution or unknown behavior.

Among the classes mentioned, tumors that required the most frequent hospitalization were acute lymphoblastic leukemias in remission or without remission, followed by malignant brain tumors or ventricular tumors (in the North, South, South-East and South-West regions), Hodgkin's nodular
sclerosis disease in the West region and mixed cellular Hodgkin's disease in Bucharest Ilfov, or malignant brain tumor in Center and North West Regions.

The analysis of the distribution of episodes of hospitalization due to tumors in children at the local level indicates, on the first positions as frequencies, counties such as Bucharest, Prahova, Mureș, Bihor, Constanța and Dolj, while at the opposite pole there are counties such as Satu Mare, Vrancea, Covasna and Botoșani - graph no.5.

Graph no.5 Distribution of hospitalisation episodes according to the patient's county of residence

In the counties with the highest number of hospitalization episodes, the most frequent types of tumors that caused hospitalization were recorded: in Bucharest - 43% of the total hospitalization episodes on the city were lymphoblastic leukemias, less than 10% Hodgkin's disease or malignant brainstem tumors. In Prahova County hospitalization episodes were most often due to acute lymphoblastic leukemia - 41% of the county total, but also to malignant brainstem tumors. In the Mureș and Bihor counties, lymphoblastic leukemia (41% and 34%) is on the first place.
In the case of the majority of counties (28), the number of these hospitalization episodes was reduced, the most significant decrease being recorded in Sălaj, Bistriţa-Năsăud and Braşov counties. The rest of the counties recorded increases, the highest in Mehedinţi county (almost double the value in 2013), Harghita with almost 75% and Hunedoara with about 50% - table no.3.

4. The distribution of hospitalization episodes due to tumors in children, depending on the patient's gender.

In terms of the patient's gender, close numbers of episodes of hospitalization due to tumors during the study period are recorded, with a slight predominance of boys (56% of total hospitalization episodes).

As a time evolution, there is a constant decrease in the number of hospitalization episodes in both sexes in 2017 compared to 2013, the observed decrease being about 15% - graph no.6.

For boys, the most frequent hospitalizations were due to malignant tumors of lymphoid, hematopoietic and related tissues, and malignant tumors of the eye, brain, and other parts of the central nervous system (85% of the total), while the tumors prevailed for the girls were of the lymphoid, haematopoietic and related tissues, and tumors with unpredictable evolution or unknown behavior (80.5% of the total).

As types of tumors, for girls, the most common types that caused hospitalization episodes during the study period were acute lymphoblastic leukemia accounting for about 37% of the total for female sex but also ovarian tumor with unpredictable and unknown evolution, Hodgkin's nodular sclerosis, malignant tumor of the cerebellum or brainstem, all with less than 10% of the total.

For male sex, the most common episodes of hospitalization were also due to acute lymphoblastic leukemia accounting for 37% of the total for this genus, but also malignant tumor affecting cerebellum and non-Hodgkin's Burkitt diffuse lymphoma in much smaller weight - tabel no.4.

5. Distribution of hospitalization episodes due to tumors in children, depending on the age of the patient.

Analyzing the structure of hospitalization episodes according to the age groups of the patients it is noted that the highest values are observed in the 5-10 years age group, approximately one third of the total hospitalization episodes due to these types of tumors during this period, but also in the groups 10-15 years and 1-5 years, one quarter each of the total - graph no.7.

Table 5 shows that the number of hospitalization episodes in most age categories was decreasing, the most significant decrease in 2017 as compared to 2013, being in the group of 1-5 years, about 25%. The age groups that registered an increase in the number of admissions were the extreme groups, the 0-1 group having the highest increase - 34%. The most significant reduction is seen in children of 5 years, almost half of the number in 2013, and the highest increase in children up to one year, more than half.
6. Distribution of hospitalization episodes due to tumors in children, depending on the patient's residence

Most of the children with episodes of hospitalization due to tumors in the period 2013-2017 come from urban areas - 15235 episodes (53%), compared with 13527 hospitalizations for rural children (47%). As a diagnostic class in the urban environment, malignant tumors of lymphoid, hematopoietic and related tumors predominate, and tumors with unpredictable development or unknown behavior (82.5% of the total in this residential environment), compared to the rural one where there are more hospitalizations for malignant tumors of lymphoid, hematopoietic and related tissues, and malignant tumors of the eye, brain, and other parts of the central nervous system.

The evolution of the number of these episodes throughout the study period was generally declining, a slightly
greater difference between the number of episodes of hospitalization registered in 2013 and that observed in 2017, with the hospitalized children coming from the urban area (15% compared to 2013).

Graph no. 9. Distribution of hospitalization episodes by development regions, depending on the patient’s residence

Table no. 6. Distribution of hospitalization episodes due to tumors in children, depending on the length of stay, 2013-2017

<table>
<thead>
<tr>
<th>Length of stay</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of days</td>
<td>53475</td>
<td>52492</td>
<td>52393</td>
<td>44872</td>
<td>47954</td>
<td>251186</td>
</tr>
<tr>
<td>Average length of stay</td>
<td>8.47</td>
<td>8.52</td>
<td>9.21</td>
<td>8.61</td>
<td>8.87</td>
<td>8.7</td>
</tr>
</tbody>
</table>

Table no. 7. Evolution of hospitalization episodes due to tumors, in children 2013-2017, depending on the patient's discharge status

<table>
<thead>
<tr>
<th>Patient’s discharge status</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worsen</td>
<td>46</td>
<td>33</td>
<td>30</td>
<td>21</td>
<td>24</td>
<td>154</td>
</tr>
<tr>
<td>Improved</td>
<td>3959</td>
<td>3963</td>
<td>3231</td>
<td>3085</td>
<td>3184</td>
<td>17422</td>
</tr>
<tr>
<td>Deceased</td>
<td>61</td>
<td>59</td>
<td>50</td>
<td>49</td>
<td>47</td>
<td>266</td>
</tr>
<tr>
<td>Stationary</td>
<td>1846</td>
<td>1753</td>
<td>1886</td>
<td>1644</td>
<td>1720</td>
<td>8849</td>
</tr>
<tr>
<td>Cured</td>
<td>397</td>
<td>348</td>
<td>488</td>
<td>410</td>
<td>428</td>
<td>2071</td>
</tr>
<tr>
<td>Total</td>
<td>6309</td>
<td>6156</td>
<td>5685</td>
<td>5209</td>
<td>5403</td>
<td>28762</td>
</tr>
</tbody>
</table>

Table no. 8. Evolution of the type of discharge in the case of hospitalization episodes due to tumors in children during 2013-2014

<table>
<thead>
<tr>
<th>Tipul externării</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decedat</td>
<td>61</td>
<td>59</td>
<td>50</td>
<td>49</td>
<td>47</td>
<td>266</td>
</tr>
<tr>
<td>Externat</td>
<td>6019</td>
<td>5908</td>
<td>5364</td>
<td>4894</td>
<td>5036</td>
<td>27221</td>
</tr>
<tr>
<td>Externat la cerere</td>
<td>77</td>
<td>79</td>
<td>83</td>
<td>71</td>
<td>87</td>
<td>397</td>
</tr>
<tr>
<td>Transfer interspitalicesc</td>
<td>152</td>
<td>110</td>
<td>188</td>
<td>195</td>
<td>233</td>
<td>878</td>
</tr>
<tr>
<td>Total</td>
<td>6309</td>
<td>6156</td>
<td>5685</td>
<td>5209</td>
<td>5403</td>
<td>28762</td>
</tr>
</tbody>
</table>

The most frequent hospitalization episodes in urban patients were determined by acute lymphoblastic leukemia (38% of all hospitalizations in this residential environment), Hodgkin’s nodular and mixed cell sclerosis (about 8%), cerebellum malignant tumor, diffuse non-Hodgkin’s Burkitt tumor or malignant brainstem tumor. The same diagnosis at admission is most common for children from rural areas. At the level of development regions, hospitalizations of children from urban areas (Bucharest Ilfov, Center, North-West, South-East and West region) predominate, while in the other regions there are more frequent hospitalizations among those living in rural areas (North-East, South and South-East) - graph no.9.

The counties with the most hospitalization episodes of the urban children caused by these three tumor classes were: Bucharest, Prahova, Brasov, Constanta, Bihor and Cluj. In the case of the other residential environment, most episodes were registered for children from Ilfov, Prahova, Dolj, Mureș, Suceava counties.

The total duration of hospitalization for admissions due to tumors in children amounted to 477225 days between 2013 and 2017, of which 251186 days (52.6%) due to the three categories of neoplasms analyzed. The number of hospitalization days has fallen steadily from 2013 to 2016 by about 16%, in 2017 recording a small increase of almost 7% over the previous year. 

The average hospitalization duration in children with tumors in the three categories studied was 8.7 days in this period, compared to the average hospitalization duration of children with neoplastic disease that was 6.64 days. Average hospitalization ranged from 8.47-9.21 days, the year with the highest average duration was 2015, and the lowest year 2013 - table no. 6. 

By tumor types, the duration of hospitalization was the highest in episodes due to malignant tumors of lymphoid, haematopoietic and related tissue (C81-C96) with an average hospitalization of approximately 10 days followed by tumors of the eye, brain and other parts of the central nervous system (C69-C72) with an average duration of 7.3 days and tumors with unpredictable evolution or unknown behavior (D37-D48) with an average duration of 5.7 days. 

Acute lymphoblastic leukemia had the highest 13.3 days of hospitalization with no mention of remission and 7.8 days with remission; other types of neoplasia long-term with high mean of hospitalization were non-Hodgkin's diffuse lymphoma Burkitt tumor - 8.4 days, cerebellum malignancy 7 days, Hodgkin's disease nodular sclerosis 6 days. The development regions with the highest average hospitalization duration were North East, West and North West, and the lowest values in the Bucharest Ilfov and the South regions, and among the counties, those with high values were Botosani (16.3 days), Bihor or Constanta (9 day values).

8. Distribution of hospitalization episodes due to tumors in children, depending on the patient's discharge status and the rate of in-hospital mortality

Most hospitalized children due to the three classes of tumors analyzed in 2013-2017 were discharged as relieved (61%), while one third were as stationary and about 7% were healed. Less than 1% of children were discharged in an aggravated state (0.5%) or died (0.9%) - graph no. 10. 

As evolution over time, there is a significant reduction over the study period of completed hospitalizations with an aggravated state of health, the number decreasing by half in 2017 as compared to 2013. The same reduction but less important is also observed in case of hospitalization episodes ended with deaths, the number decreasing by 23% compared to 2013-table no 7. 

Table no.7 Evolution of hospitalization episodes due to tumors, in children 2013-2017, depending on the patient's discharge status 

Most deaths occurred in children with malignant lymphoid, haematopoietic and related tissue tumors (62% of all deaths) and those with malignant tumors of the eye, brain, and other parts of the central nervous system (30%). In terms of diagnosis at admission, most of the deaths were observed in children with acute lymphoblastic leukemia diagnosis, with no mention of remission (17.3% of all deaths), acute myeloid leukemia, without mention of remission (8.6 %), acute lymphoblastic leukemia in remission (5.6%), or malignant tumor of the brainstem (4.9%). 

North-East and North-West have the highest deaths (22% and 15% of all deaths nationwide) and the least occurred in West region (6.4%). At the local level, most deaths due to these three types of tumors were found in Bucharest (8.3% of the national total), Iasi (5.6%) and Suceava (4.5%). 

95% of the total hospitalization episodes due to tumors in children were completed with normal discharges, while 3% represented in-hospital transfers, and 1.4% discharges on demand - graph no. 11.

Compared to the initial year, over the last year of the study period there was an increase of over 65% in the case of interhospital transfers and also a lower (approximately 13%) increase in the number of inpatient episodes completed by a discharge on-demand - table no.8. In-hospital mortality rates were 0.92% throughout the entire period, ranging from 0.96% in 2013 to 0.87% in 2017.

Conclusions

Following the analysis, processing and interpretation of DRG data over the last 5 years, regarding hospitalization due to the main / most common three categories of tumors that affected patients aged 0-18 years, we can conclude that:

- Of the 71824 episodes of hospitalization due to tumors in children 0-18 years during the period 2013-2017, the three tumor categories that most affected the children, causing the highest number of admissions, representing 40% of the total, were in order: malignant tumors of lymphoid, hematopoietic and related tissues, malignant tumors of the eye, brain and other parts of the central nervous system, and tumors with unpredictable evolution or unknown behavior;

- Of the 28762 hospitalizing episodes, malignant tumors of lymphoid, haematopoietic and related tissues caused about more than half of admissions, malignant tumors of the eye, brain and other parts of the central nervous system about one fifth, and tumors with unpredictable development or unknown behavior approx. one fifth. The results obtained in this study confirm the international statistics according to which the first two categories represent the most frequent impairment in children and adolescents;

- The evolution study indicates a general downward trend, which is only valid for malignant tumors of the lymphoid, haematopoietic and related tissue, and partly for malignant tumors of the eye, brain and other parts of the central nervous system. For tumors with unpredictable development or unknown behavior, the number of hospital episodes has increased over the last years of the study period as compared to 2013;

- Of the haematopoietic and lymphoid tumors, the most common was acute or myeloid lymphoblastic
leukemia or lymphoma, in terms of tumors of the nervous system, mainly brain tumors affecting cerebellum or brainstem, and in the category of unpredictable tumors or unknown behaviors are ovarian tumors;

- Evolution throughout the study period was a downward trend in the case of blood or lymphatic system tumors, but with respect to the other categories, a higher number of hospitalizations (even doubles) was observed, especially in the case of unpredictable tumors such as those of the ovary or some brain tumors so classified;

- Case studies at national level, by development region, show a uniform distribution with close values between regions, except for the extremes: the South Region with the highest number of hospitalizations and the lowest number in West;

- The evolution trend was a downward trend for all regions, with two exceptions: the West region with more than one fifth increase in 2017 compared to the initial year and the Center region;

- At the local level, the counties of Bucharest and the counties of Prahova, Mureș, Bihor, Constanța and Dolj were the leading counties;

- As a local trend in 28 counties, the number of hospitalizations decreased compared to the one recorded in the initial year of the study, while in the rest are observed increases, the highest in counties like Mehedinți (almost double), Harghita and Hunedoara;

- The most frequent episodes of hospitalization were recorded by boys (more affected by this disease according to international and national statistics) but the trend was decreasing;

- As tumor classes, both sexes were primarily affected by haematopoietic and lymphatic tumors, but if boys develop more frequently brain tumors, in girls predominate those with unpredictable evolution; Leukemias and lymphomas predominate in both sexes;

- From the age point of view, 5-10 years predominate as one-third of all episodes; the trend over time has been declining in all other age groups except for extreme groups, with children under 1 year of age accounting for the most significant increase over one third;

- Leukemias, lymphomas and brain tumors predominate in all age groups;

- Inpatient duration analysis indicates a number of days of hospitalization by these three tumor categories, representing more than half of the total days of admissions caused by tumors; however, the number of these days was reduced in 2017 compared to 2013 by about 16%; The average of hospitalization in these categories exceeds hospitalization by tumors, ranging from 8.47-9.21 days;

- Children with hematopoietic tumors (10 days on average) hospitalized for most of the time almost double of those with brain tumors, and leukemia counts most in the premium category as duration of admission;

- From the point of view of the state of admission, very small percentages were discharged as aggravated or deceased (less than 1%), and their number continued to decrease over time;

- As a mortality rate for in-hospital mortality, it was overall 0.92% higher than that determined by tumors in general (0.5%) and varied over the period with values between 0.96% in 2013 and 0.87% in 2017.

In order to make comparisons and formulate effective interventions, the lack of data at both national and international level was the main problem of this study.

**Bibliografie**