MORBIDITY AND DEATHS DUE TO LEUKEMIA IN PATIENTS UNDER 14 YEARS

MORBIDADE E ÓBITOS POR LEUCEMIA EM MENORES DE 14 ANOS

MORBILIDAD Y MUERTES POR LEUCEMIA EN MENORES DE 14 AÑOS

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ABSTRACT

Objective: to analyze the temporal and behavioral trend of hospital morbidity and deaths due to leukemia in children under 14 years of age. **Method:** this is a quantitative, retrospective study with data provided by the Department of Informatics of the Unified Health System (DATASUS), from 2008 to 2016. Data was collected through a form. The percentage rates were then calculated and then supported with a spreadsheet (Excel) for linear regression analysis. Results were presented in the form of tables. **Results:** the analysis of trends in hospital morbidity and deaths showed different profiles, with an oscillatory pattern in both values and low mortality rates. **Conclusion:** due to the agility in the access to the specialized health service, it was defined the improvement of the prognosis and increased the chances of survival of patients with leukemia under 14 years of age, making possible low leukemia mortality rates in the municipality. **Descriptors:** Leukemia; Morbidity; Cancer; Childhood; Hospitalization; Neoplasia.

RESUMO

Objetivo: analisar a tendência temporal e comportamental da morbidade hospitalar e óbitos por leucemia, em menores de 14 anos de idade. **Método:** trata-se de estudo quantitativo, retrospectivo, com dados disponibilizados pelo Departamento de Informática do Sistema Único de Saúde (DATASUS), de 2008 a 2016 e coletados por meio de formulário. Calcularam-se as taxas percentuais que, em seguida, foram conduzidas com o apoio de uma planilha eletrônica (Excel) para a análise por regressão linear. Apresentaram-se os resultados em forma de tabelas. **Resultados:** apresentaram-se, pela análise da tendência para a morbidade hospitalar e óbitos, perfis distintos, com um padrão oscilatório nos valores para ambos e baixos índices de mortalidade. **Conclusão:** definiu-se, pela agilidade no acesso ao serviço de saúde especializado, a melhora do prognóstico e aumentaram-se as chances de sobrevivência dos pacientes portadores de leucemia menores de 14 anos de idade, viabilizando baixas taxas de mortalidade por leucemia no município. **Descritores:** Leucemia; Morbidade; Câncer; Infância; Hospitalização; Neoplasia.

RESUMEN

Objetivo: analizar la tendencia temporal y conductual de la morbilidad hospitalaria y las muertes por leucemia en menores de 14 años de edad. **Método:** se trata de un estudio cuantitativo, retrospectivo, con datos proporcionados por el Departamento de Informática del Sistema Único de Salud (DATASUS), en el período de 2008 a 2016. Se realizó la recolección de datos por medio de formulario. Se calcularon las tasas porcentuales que luego se realizaron con el apoyo de una hoja de cálculo (Excel) para el análisis por regresión lineal. Se presentaron los resultados en forma de tablas. **Resultados:** se presentaron, por el análisis de la tendencia a la morbilidad hospitalaria y muertes, perfiles distintos, con un patrón oscilatorio en los valores para ambos y bajos índices de mortalidad. **Conclusión:** se definió, por la agilidad en el acceso al servicio de salud especializado, la mejora del pronóstico y se aumentaron las posibilidades de supervivencia de los pacientes portadores de leucemia menores de 14 años de edad, viabilizando bajas tasas de mortalidad por leucemia en el municipio. **Descritores:** Leucemia; Morbilidad; Cáncer; Infancia; Hospitalización; Neoplasias.

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INTRODUCTION

Cancer is a serious public health problem with a tendency to increase cases. It has a high impact on family, children and public resources, requiring the development of strategies that aim at the best application of resources, early detection and prevention at the possible limit of complications since, to date, it is not a preventable disease in children in early childhood and studies of genetic and environmental factors are still few and are ongoing to determine causes.¹⁻⁴

Cancer is characterized by loss of control of cell division and the ability to invade other organic structures. It is defined, in children, from its morphology and should not be studied as cancer in adults, defined from the primary site of origin. This differentiation arises due to distinct clinical behaviors, in which the latency period is shorter, and although this type of cancer is more invasive, growing rapidly, it responds better to treatment. It is known that leukemia is one of the most frequent types of tumors in childhood and adolescence, as well as neoplasms of the central nervous system and lymphomas, acute lymphoid leukemia constitutes approximately one third of the malignant neoplasms of the child.⁵⁻⁷

It is reported that the main type of leukemia in childhood is acute lymphocytic leukemia (ALL), a malignant disease that affects leukocytes, causing a change in cellular morphology, characterized mainly by the exaggerated production of abnormal young cells in the bone marrow. Due to this anomaly, the production of other normal blood components (red blood cells, leukocytes and platelets) is impaired, predisposing to anemia, infections and hemorrhages, and contributing to the prolongation of hospitalization time of cancer patients.⁴

It can be observed that the clinical presentation of ALL is quite unspecific and may delay the diagnosis, since, in ALL, the most frequent signs and symptoms are fever of infectious cause, adenomegaly, ecchymosis and pallor, and may also present joint and bone pain in the lower limbs, and fatigue, apathy, anorexia, mucosal bleeding, and increased abdominal volume due to hepatosplenomegaly.⁸

The etiopathogenesis of leukemia in infants is associated with genomic aberrations (translocations, deletions or duplications of segments or the entire chromosome). It may lead to the development of ALL in the fetal phase by the use of contraceptives during pregnancy, and the probable cause would be a genetic change in the organism of the fetus by exposure of the mother to the hormone estrogen, which can deform a gene called MLL (*Mixed Lineage Leukemia*).^{3,9} This genetic mutation occurs in a protein called interleukin 7, or IL7R, responsible

for the maturation of T lymphocytes. It leads, by its continuous activation, to the exaggerated proliferation of immature lymphocytes and to the development of ALL.⁹⁻¹¹

It is fundamental to survey the death rates and hospital morbidity indexes for data monitoring and evaluation of health services, as well as the analysis of regional time trends. It is inferred that this information can help in the planning of measures and provide subsidies for the implementation of actions of managers and interventions directed to the needs of that specific group.¹

OBJECTIVE

- To analyze the temporal and behavioral trend of hospital morbidity and leukemia deaths in children under 14 years of age.

METHOD

This is a quantitative, retrospective, trend analysis study on hospital morbidity and deaths from leukemia in children under 14 years of age in the municipality of Montes Claros-MG, with information provided by the Ministry of Health on the DATASUS website, and other types of neoplasms and other age groups.¹²

It was estimated that the estimated population for the municipality in 2017 is 402,027 inhabitants and the Municipal Human Development Index, classified as 0.770, in 2010. Two main specialized units with Hospital Registry of Cancer in the municipality (RHC), being the Brotherhood of Our Lady of Mercy - Santa Casa de Misericórdia de Montes Claros, located in Honorato Alves square, and Prontoclínica and Hospital São Lucas, located at Avenida Geraldo Athayde, 480 - São João. It is revealed that these two hospitals are reference for cancer treatment of all the cities of the north of Minas Gerais composed of more than one hundred municipalities.¹³⁻¹⁴

A form constructed by the researchers was used for data collection and the period used in the study was nine consecutive years, between 2008 and 2016, considering two large dependent variables, hospital morbidity and deaths, and their independent variables: year, age, gender and race. Children and adolescents were distributed in the age groups: less than one year; from one to four; from five to nine; from ten to 14, separated according to sex and race (white, black, brown, yellow, indigenous and with no information).¹²

Percentage rates were calculated by conducting them with the aid of a spreadsheet (Excel) for linear regression analysis. For the findings, the possible correlations between their behavior and the time series were verified by means of linear regression, assuming a significance level of 5% (p <0.05).¹⁵

Secondary data in the public domain have been used in this study, so there is no direct contact with the patient or his / her personal data, and the data consulted is available to all persons who are willing to consult them. It is added, therefore, that it is not necessary to submit this project to the research ethics committee, as it does not involve direct contact with humans and animals, as well as the identification of the participants, as it does not hurt ethical care, falls within

Resolution 466 of 2012, of the National Health Council (NHC).¹⁶

RESULTS

Data was analyzed for 815 children who were hospitalized during the study period (2008 to 2016), of whom 31 died of leukemias. The analysis of the trend for hospital morbidity and the different profile profiles were presented, with an oscillatory pattern in the values for both (Table 1).

Table 1. Number of cases of hospital morbidity and deaths due to leukemia in children under 14, between 2008 and 2016. Montes Claros (BR), Brazil, 2017.

Yes	Total		Distribution by age group							
	Hospital morbidity	Deaths	< than 1 year		1 to 4 years		5 to 9 years		10 to 14 years	
			*M	*D	*M	*D	*M	*D	*M	*D
2008	61	3	0	0	14	0	34	1	13	2
2009	87	6	4	0	37	2	28	1	18	3
2010	119	2	0	0	12	0	64	1	43	1
2011	72	5	0	0	25	0	35	2	12	3
2012	68	3	1	0	21	1	37	1	9	1
2013	89	4	0	0	30	1	53	2	6	1
2014	120	3	0	0	66	0	32	2	22	1
2015	94	2	0	0	26	0	37	0	31	2
2016	105	3	1	1	25	0	51	1	28	1

Source:¹² *M: Leukemia morbidity *D: Death by leukemia

During the study period, leukemia mortality rates in children under 14 years of age ranged from 4.41% to 6.94%, and the values with the highest statistical significance were in the years 2009 and 2011, where the highest rates were

observed, respectively 6.90% and 6.94%, and the year with the lowest rate was 2010, with the percentage of 1.68%. The rate below 3% has been maintained in the last three years (Table 2).

Table 2. Leukemia mortality rate in children under 14, between 2008 and 2016. Montes Claros (MG), Brazil, 2017.

Year	Number of cases of hospital morbidity F(n)	Number of deaths F(n)	Mortality rate F(%)
2008	61	3	4.92
2009	87	6	6.90
2010	119	2	1.68
2011	72	5	6.94
2012	68	3	4.41
2013	89	4	4.49
2014	120	3	2.50
2015	94	2	2.13
2016	105	3	2.86

Source:¹²

It can be observed that the years 2010 and 2014 have a greater number of cases referring to hospital morbidity, with 119 and 120 cases, respectively. In terms of gender segregation, it was observed a higher incidence for males when compared to females, except in 2011 and 2012, in which the percentages reached the most

significant values for females, in the year 2011, they reached 18 cases more than in the previous year (Table 3).

The number of deaths was oscillated in both sexes, and the years 2009, 2011, 2013 stood out, doubling and increasing from the previous year's value to the female (Table 3).

Table 3. Number of cases of hospital morbidity due to leukemia and distribution by sex, between 2008 and 2016. Montes Claros (MG), Brazil, 2017.

Year	Children under 14 years of age			Persons aged 15 years or over		
	Total number of hospital morbidity cases	Percentage distribution by sex		Total number of hospital morbidity cases	Percentage distribution by sex	
		Male n	Female n		Male n	Female N
2008	3	2	1	61	36	25
2009	6	2	4	87	63	24
2010	2	2	0	119	87	32
2011	5	3	2	72	22	50
2012	3	2	1	68	25	43
2013	4	1	3	89	51	38
2014	3	2	1	120	68	52
2015	2	2	0	94	56	38
2016	3	2	1	105	67	38

Source:¹²

The brown breed was more affected by the disease and, consequently, has the highest number of deaths, except for the years 2011 and 2013 in

which there was no information about the sex of the children (Table 4).

Table 4 - Number of cases of hospital morbidity and death by leukemia according to race, between 2008 and 2016. Montes Claros (MG), Brazil, 2017.

Year	Children under 14 years of age													
	Total Hospital Morbidity	Death	Distribution by colour or race										Without information	
			White		Brown		Black		Yellow		Indigenous			
			*M	*D	*M	*D	*M	*D	*M	*D	*M	*D		
2008	61	3	5	0	54	2	0	0	0	0	0	0	2	1
2009	87	6	7	0	76	6	0	0	0	0	0	0	4	0
2010	119	2	4	0	108	2	0	0	0	0	0	0	7	0
2011	72	5	19	0	46	2	0	0	0	0	0	0	7	3
2012	68	3	5	3	35	2	0	0	0	0	0	0	28	0
2013	89	4	3	0	53	1	0	0	0	0	0	0	33	3
2014	120	3	13	1	104	2	0	0	0	0	0	0	3	0
2015	94	2	2	0	87	2	0	0	0	0	0	0	5	0
2016	105	3	16	1	83	2	0	0	0	0	0	0	6	0

Source:¹² *M: hospital morbidity due to leukemia; *D: death by leukemia

DISCUSSION

It is observed that the oscillation in leukemia mortality rates in children under 14 years of age, verified in the municipality of Montes Claros, is in agreement with similar results ascertained in the literature for some cities in the Northeast of the country and in the poorest regions where the indices are are controlled and, in this sense, were discordant with what has been reported in other localities of the country, such as Rio de Janeiro, Goiânia, São Paulo and Belo horizonte, in which mortality rates due to leukemia have declined a lot in recent years.^{6,17-8}

There is an oscillation in the mortality rates of the conflict between positive and negative factors. It is explained that the positive factors are advances in the treatments by combining the use of chemotherapy, radiotherapy and bone marrow transplantation (indicated in only a few cases) and the standardization of protocols proposed by the Ministry of Health, in an effort to increase detection precoce of neoplasias, resulting in an increase in the survival of the affected children. Negative factors are related to extrinsic

factors, such as instability of effectiveness in health care, increase in cases proportional to population increase, absence of studies on causal factors in children of second childhood, among others.^{15,17}

It was found that the incidence of leukemia is higher in male children and the number of deaths is also higher, except for the years 2009 and 2013, in which the female had higher percentages. Similar results were found regarding sex, predominantly male, with a higher incidence of leukemia diagnosis.¹⁹⁻²⁰

The mortality rate for low leukemia is considered and it oscillated several times, with periods of increase and decline between values, and, when compared the number of deaths with the number of cases of hospital morbidity, the values are discrepant. It can be observed that hospital morbidity, despite tending to increase progressively due to population growth and lack of definition of causal factors, did not obey standards during the nine years analyzed (Graph 1), while the number of deaths is low despite significant values of hospital morbidity. It should be noted that the evolution of the treatments plays a

fundamental role for the improvement of the prognosis and decrease of the recidivism,

generating greater effectiveness and less negative events due to the side effects of the drugs used.^{1,5}

Figure 1. Hospital morbidity and deaths from leukemia (2008 to 2016)

Source:¹²

The studies showed that the five- to nine-year and ten to 14-year age groups have higher mortality rates, as well as the brown and white breeds are more susceptible to the disease, however, when considered that some children did not have that Brazil is a predominantly mixed-gender country, it is unclear to guarantee a single specific race for the majority of the population, so it is impossible to say that children of the black, indigenous and yellow races are not affected by the disease.^{14,19}

The data in this research are generally presented as consistent, since the data provided by the Ministry of Health are reliable and served as a subsidy for the elaboration of strategies aimed at this specific group, as well as a source of information for future work.

CONCLUSION

The improvement of the prognosis was improved due to the agility in the access to the specialized health service, and the chances of surviving leukemia patients under 14 years of age in the municipality of Montes Claros - Minas Gerais were increased. The low mortality rates in the municipality were feasible for diagnosis and treatment, so it is important to emphasize that, in order to maintain lower values, these should occur in the initial phase of the disease and, considering that not all children have access to specialized centers and travel costs can be high, especially for people living in rural areas and cities farther away, leading to the abandonment of treatment at the remittance stage and causing recidivism, it is necessary to develop mechanisms in the UHS that enable the children and their families to have access to treatment success.

Studies have shown that the indices do not follow well defined patterns, however, it has been noted that the older the age, the worse the prognosis, and the brown and white races are more susceptible to the disease, despite the particularities discussed in the study.

It is believed that this trend analysis is an indicator of the effectiveness of the intervention strategies of the municipality against leukemia in the treatment and early diagnosis question, and it

can be affirmed that the maintenance of low mortality rates directly portrays the effectiveness of health care.

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