Demographic and Clinical Profile of Cases of Hematological Neoplasms in Children and Adolescents

doi: https://doi.org/10.32635/2176-9745.RBC.2022v68n2.2356

Perfil Demográfico e Clínico de Casos de Neoplasias Hematológicas em Crianças e Adolescentes

Perfil Demográfico y Clínico de Casos de Neoplasias Hematológicas en Niños y Adolescentes

Lucele Gonçalves Lima Araújo[1]; Vandilson Pinheiro Rodrigues[2]; Melaine Mont'Alverne Lawall Silva[3]; Gabrielle Cristinne Alves Azevedo[4]; Pablo de Matos Monteiro[5]; João Marcelo Saraiva Ferreira[6]; Huderson Macedo de Sousa[7]

ABSTRACT

Introduction: Hematological cancers are important causes of death in childhood and adolescence. **Objective:** To design the demographic and clinical profile of cases of hematological cancer reported for children and adolescents in a referral hospital in the city of São Luís, Maranhão, Brazil. **Method:** A retrospective observational study with secondary data collected from medical records of bone marrow tumor cases in patients aged up to 19 years registered in a public referral hospital for cancer treatment from 2005 to 2015. Patient's profile was collected in addition to follow-up data. The chi-square and Fisher's exact test were used in the statistical analysis. The significance level was 5% (p<0.05). **Results:** Cases of death were higher in patients diagnosed with non-Hodgkin's lymphoma. Most patients with lymphoid leukemia were males aged up to 5 years, and the frequency of death in patients with lymphoid leukemia was lower in confirmed cases of type B lymphoblastic precursor cell leukemia when compared to the other categories. **Conclusion:** The findings suggest that most patients aged up to 19 years diagnosed with lymphoid leukemia were males and aged up to 5 years old.

Key words: hematologic neoplasms; demography; mortality; child; adolescent.

RESUMO

Introdução: As neoplasias hematológicas são importantes causas de morte na infância e adolescência. **Objetivo:** Caracterizar o perfil demográfico e clínico de casos notificados de neoplasias hematológicas em crianças e adolescentes em um hospital de referência do município de São Luís, Maranhão, Brasil. **Método:** Estudo observacional retrospectivo com dados coletados de prontuários médicos de casos de neoplasias hematológicas em pacientes com idade até 19 anos registrados em um hospital público de referência para tratamento oncológico, no período de 2005 a 2015. Foram coletados dados de caracterização geral dos pacientes e dados do seguimento do tratamento. Os testes qui-quadrado e exato de Fisher foram utilizados na análise estatística. O nível de significância adotado foi de 5% (p<0,05). **Resultados**: Os casos de óbito foram mais elevados nos pacientes diagnosticados com linfoma não Hodgkin. A maioria dos pacientes com leucemia linfoide era do sexo masculino com idade até 5 anos, e a frequência de óbito nos pacientes com leucemia linfoide foi mais baixa nos casos confirmados de leucemia linfoblástica de células precursoras tipo B quando comparado às outras categorias. **Conclusão:** Os achados sugerem que a maioria dos pacientes com até 19 anos diagnosticados com leucemia linfoide era do sexo masculino e com idade até 5 anos.

Palavras-chave: neoplasias hematológicas; demografia; mortalidade; criança; adolescente.

RESUMEN

Introducción: Las neoplasias hematológicas son causas importantes de muerte en la niñez y la adolescencia. **Objetivo:** Caracterizar el perfil demográfico y clínico de los casos notificados de neoplasias hematológicas en niños y adolescentes en un hospital de referencia de la ciudad de São Luís, Maranhão, Brasil. **Método:** estudio observacional retrospectivo con datos secundarios recolectados de registros médicos de casos de tumores de médula ósea en pacientes de hasta 19 años registrados en un hospital público de referencia para tratamiento de cáncer de 2005 a 2015. Se recolectaron datos de caracterización. Datos generales de pacientes y seguimiento -up datos. En el análisis estadístico se utilizaron las pruebas de chi-cuadrado y exacta de Fisher. El nivel de significancia adoptado fue del 5% (p<0,05). **Resultados:** Los casos de muerte fueron mayores en pacientes con diagnóstico de linfoma no Hodgkin. La mayoría de los pacientes con leucemia linfoide eran varones de hasta 5 años, y la frecuencia de muerte en pacientes con leucemia linfoide fue menor en los casos confirmados de leucemia de células precursoras linfoblásticas tipo B en comparación con las otras categorías. **Conclusión:** Los hallazgos sugieren que la mayoría de los pacientes de hasta 19 años diagnosticados con leucemia linfoide eran hombres y tenían hasta 5 años.

Palabras clave: neoplasias hematológicas; demografía; mortalidad; niño; adolescente.

[1-7]Universidade Federal do Maranhão (UFMA). São Luís (MA), Brazil.
[1]E-mail: lucele.araujo@ufma.br. Orcid iD: https://orcid.org/0000-0003-1725-9038
[2]E-mail: vandilson.rodrigues@ufma.br. Orcid iD: https://orcid.org/0000-0002-6785-7864
[3]E-mail: melaine.lawall@ufma.br. Orcid iD: https://orcid.org/0000-0003-4773-1612
[4]E-mail: gabrielle.azevedo@discente.ufma.br. Orcid iD: https://orcid.org/0000-0002-7737-9456
[5]E-mail: pm.monteir@discente.ufma.br. Orcid iD: https://orcid.org/0000-0002-3879-5326
[6]E-mail: joao.saraiva@discente.ufma.br. Orcid iD: https://orcid.org/0000-0002-1980-7694
[7]E-mail: huderson.macedo@discente.ufma.br. Orcid iD: https://orcid.org/0000-0003-2786-6253
Corresponding author: Lucele Gonçalves Lima Araújo. Departamento de Morfologia da UFMA. Avenida dos Portugueses, 1966 – Vila Bacanga. São Luís (MA), Brazil. CEP 65080-805. E-mail: lucele.araujo@ufma.br

INTRODUCTION

Leukemias, hematopoietic system cancers, are considered important causes of death in children and adolescents[1,2], they are characterized by the accumulation of altered cells in the bone marrow[3], while lymphomas are cancers originated from the lymphatic system[4]. Typically, these pathologies result from cumulative cells alterations causing signs and symptoms as anemia, weakness, fever, paleness and discouragement, cervical, axillary, inguinal adenomegaly among others. However, the symptomatology of leukemias occur when there is dissemination of neoplastic cells into lymphatic ganglia[4], different from lymphoma, whose adenomegaly is an initial symptom[5].

Lymphoblastic lymphoma and lymphoblastic leukemia can be originated from lineages of lymphocytes B or T described in the International Classification of Diseases and Related Health Problems (ICD-10)[6] with separate codes, and ambiguity of terms regarding cellular lineage, usually being utilized the term *unspecified cell site* (UCS) for cases without evidences of cellular changes of these cancers[7,8]. According to the world estimate for 2017, 249 thousand new cases of leukemia, 510 thousand new cases of non-Hodgkin's lymphoma and 79 thousand new cases of Hodgkin's lymphoma occurred. Australia, New Zealand, North America and European Regions reported higher incidence rates[9,10].

Lymphomas and leukemias are the most frequent hematological neoplasms in children and adolescents[11,12]. Epidemiological data showed that 4,795 deaths by leukemia and nearly 5,123 deaths by Hodgkin's and non-Hodgkin's lymphoma occurred in 2017[13] in Brazil.

It is anticipated from 2020 to 2022, 5,920 new cases of leukemia, 6,580 new cases of non-Hodgkin's lymphoma and 1,590 of Hodgkin's lymphoma for men and 4,890, 5,450 and 1,050 for women, respectively[13]. The World Health Organization (WHO) affirms the possibility of an increase of 81% in the incidence of cancer in developing and underdeveloped countries where mortality exceeds survival, being imperative to count with diagnostic services at health basic attention[14].

In addition. diagnosis and treatment of cases of childhood and adolescents hematological neoplasms impact the entire family, causing fear, depression and anxiety because of concerns with the diagnosis, treatment, control and outcome. Death is an imminent possibility in this setting, indicating that investments in early control of these neoplasms for this population are necessary within the scope of health global coverage[14,15].

The objective of the present study was to characterize the cases of hematological neoplasms in children and adolescents registered at an oncologic treatment reference hospital in a capital of the Northeast region to help health professionals and managers in planning public health policies.

METHOD

Retrospective, observational study with data collected from the charts at the Cancer Hospital Registry (CHR) of "*Hospital do Câncer Aldenora Bello (HCAB)*", reference of oncologic treatment in the municipality of São Luís, capital of the state of Maranhão, Brazil, approved by the Institutional Review Board of "*Universidade Federal do Maranhão*" number CAAE: 84791617.0.0000.5087.

Data of individuals of both genders aged up to 19 years old with confirmed diagnosis of hematological neoplasm submitted to antineoplastic therapy and followed-up in the same hospital from 2005 to 2015 were included. Data from patients who were treated in other health clinics and missing data in the diagnosis were excluded. The total sample consisted in 409 patients distributed as follows: 245 cases of acute lymphoblastic leukemia, 55 cases of acute myeloid leukemia, 41 cases of Hodgkin's lymphoma, 22 of non-Hodgkin's lymphoma and 46 with other types of hematological neoplasms.

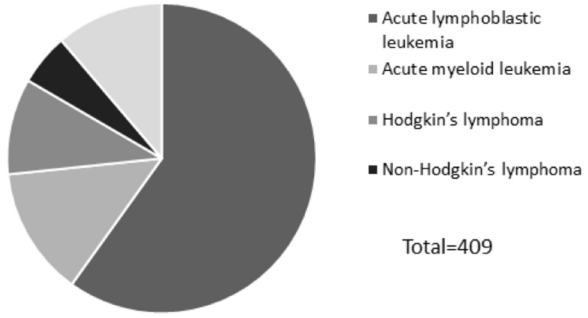
Data were extracted from the hospital's Tumor Log Form. The variables were: general data (sex, age and origin), diagnosis of the neoplasm, histological type, type of treatment, blasts, blood type, outcome of the treatment).

The Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM, Chicago, IL, USA) was utilized for statistical analysis. Initially, descriptive analysis through measures of absolute and relative frequency, measures of central tendency and measures of dispersion were calculated. The conventional chi-square tests (χ^2) or Fisher exact test were utilized in the comparative analysis of frequencies. The level of significance adopted was 5% ($p<0.05$). Results were presented as tables and graphs.

RESULTS

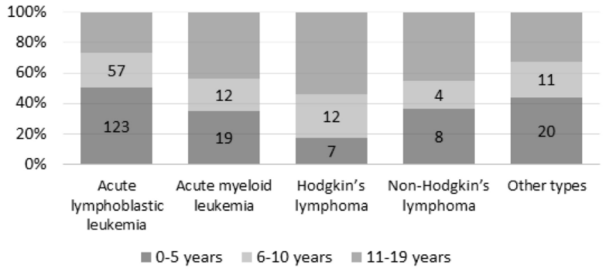
409 charts of patients with hematologic neoplasms and age up to 18 years old were included, 245 of which (60%) were cases of acute lymphoblastic leukemia and the second more incident was acute myeloid leukemia with 55 cases (14%) as portrayed in Graph 1.

Graph 2 shows the distribution and comparative analysis of age-ranges according to the type of hematologic neoplasm. Statistically significant difference was found in the distribution of age-ranges according to the type of tumor ($p=0.003$). The cases of acute lymphoblastic



Graph 1. Distribution of cases collected according to diagnosis (ICD-10)

leukemia occurred more frequently in patients aged up to 5 years old (50.2%) and the cases of acute myeloid leukemia, Hodgkin's disease and non-Hodgkin's lymphoma were more frequent in the age range of 11-19 years old.



Graph 2. Distribution of hematological malignancy cases according to age-ranges (p=0.003)

Table 1 revealed that deaths were statistically higher (p<0.001) in patients diagnosed with non-Hodgkin's lymphoma (68.2%) and acute myeloid leukemia (65.5%) when compared to patients with Hodgkin's lymphoma (19.5%).

The distribution of the variables of general characterization and association with the evolution of the case in patients with acute lymphoblastic leukemia is presented in Table 2. The sample of patients with acute lymphoblastic leukemia consisted mostly of male patients (60.8%), up to 5-years of age (50.2%), living in the state's rural area (70.6%), who submitted to chemotherapy treatment alone (58%) and blood type O (35.9%). It was found significant association (p<0.001) only with the variable type of treatment. The cases of death were higher in patients treated with chemotherapy combined with radiotherapy (93.8%).

In addition, the histological type has also influenced the evolution of the case (p=0.004). The frequency of death was lower in the cases confirmed of precursor B-cell lymphoblastic leukemia compared to other categories (Table 3).

DISCUSSION

The analysis of the hematological indicators in children and adolescents can help to monitor their health condition, encourage epidemiologic findings and development of new therapeutic alternatives to cope with this group of diseases[15]. The findings of this study suggest higher frequency of acute lymphoblastic leukemia, followed by acute myeloid leukemia corroborating the literature[16].

The cases of acute lymphoblastic leukemia occurred more frequently in patients aged up to 5-years old and for acute myeloid leukemia, Hodgkin's lymphoma and non-Hodgkin's lymphoma most of the cases occurred in the age-range of 11-19 years old, similar to the literature[17]. However, as there is no consensus yet about the actual cause of this prevalence in the first infancy, it can be considered a manifestation of genetic alterations triggering acute lymphoblastic leukemia[18-23].

Promising results have been achieved in the treatment of acute lymphoblastic leukemia with survivorship of

Table 1. Distribution of the evolution of the treatment according to the type of hematologic neoplasm

Variables	Evolution of the treatment				p
	Survival		Death		
	n	(%)	n	(%)	
ICD at diagnosis					<0.001*
Acute lymphoblastic leukemia	126	(51.4)	119	(48.6)	
Acute myeloid leukemia	19	(34.5)	36	(65.5)	
Hodgkin's lymphoma	33	(80.5)	8	(19.5)	
Non-Hodgkin's lymphoma	7	(31.8)	15	(68.2)	
Other types	21	(45.6)	25	(54.4)	

Caption: ICD-10 = International Classification of Diseases and Related Health Problems.

(*) Statistically significant difference by chi-square test (p<0.05).

Table 2. Distribution of the frequencies of the variables of general classification according to the evolution of the treatment of the cases diagnosed with acute lymphoblastic leukemia

Variable	Total		Evolution of the treatment				p
			Survival		Death		
	n	(%)	n	(%)	n	(%)	
Sex							0.452
Male	149	(60.8)	80	(53.7)	69	(46.3)	
Female	96	(39.2)	46	(47.9)	50	(52.1)	
Age at diagnosis							0.552
0-5 years	123	(50.2)	67	(54.5)	56	(45.5)	
6-10 years	57	(23.3)	29	(50.9)	28	(49.1)	
11-19 years	65	(26.5)	30	(46.1)	35	(53.9)	
Origin							0.862
São Luís	68	(27.8)	38	(55.9)	30	(44.1)	
Countryside	173	(70.6)	86	(49.7)	87	(50.3)	
Off state cities	2	(0.8)	1	(50.0)	1	(50.0)	
Not informed	2	(0.8)					
Type of treatment							<0.001*
CT	142	(58.0)	41	(28.9)	101	(71.1)	
CT + RT	17	(6.5)	1	(6.2)	15	(93.8)	
CT + RT + surgery	6	(2.4)	6	(100)	0	(0)	
Not informed	81	(33.1)					
Blasts							0.417
0-20%	152	(62.0)	57	(37.5)	95	(62.5)	
> 20%	16	(6.6)	4	(25.0)	12	(75.0)	
Not informed	77	(31.4)					
Blood type							0.603
A	51	(20.8)	17	(33.3)	34	(66.7)	
B	13	(5.3)	3	(23.1)	10	(76.9)	
AB	3	(1.2)	0	(0)	3	(100)	
O	88	(35.9)	27	(30.7)	61	(69.3)	
Not informed	90	(36.7)					

Captions: MA = State of Maranhão; CT = chemotherapy; RT = radiotherapy.

(*) p<0.05.

Table 3. Association between evolution of the treatment and the histological type of the tumor in patients with acute lymphoblastic leukemia

Variables	Evolution of the treatment				p
	Survival		Death		
	n	(%)	n	(%)	
Histological type of the tumor					0.004*
Precursor cell lymphoblastic leukemia, UCS	84	(45.9)	99	(54.1)	
Precursor B-cell lymphoblastic leukemia	11	(84.6)	2	(15.4)	
Other types	31	(63.3)	18	(36.7)	

Caption: UCS = unspecified cell site.

(*) p<0.05.

90%, reducing substantially the acute levels of delayed morbidities, providing correct medications to more resistant subclassifications in distinct population groups ensuring better quality of life to patients in developed countries[24,25], although this still appears to be far from the reality of countries in development[26,27]. In addition, the familial etiological germinative investigations for the development of leukemias in children and adolescents should be conducted earlier and effectively because of the evaluation of new entities of acute myeloid leukemia with genetic mutations[28].

The findings of this study showed higher frequency of death in patients with non-Hodgkin's lymphoma (68.2%) and acute myeloid leukemia (65.5%) when compared to patients with Hodgkin's lymphoma (19.5%). With this reality, apparently the countries in development have difficulties to access specialized medical clinics, medical tests, proper therapies and compatible with the current necessity, with potential to impact the survival rates[16,27,29-32]. Furthermore, in 2017, at the admission to the National Health System (SUS) it was noticed that the oncologic support for acute lymphoblastic leukemia was counted as first cause of death by disease with rate from 2% to 4% of the new cases compared to all lymphomas and leukemias[27,33-35].

Between 1980 and 2015, the percentage of mortality by leukemia of children and adolescents in the capitals of the Brazilian states declined according to the study of mortality trends by leukemia[33-35]. Survival rate of patients with acute lymphoblastic leukemia corresponds to 64% with regional variations across Brazilian cities, different from developed countries where the percentage exceeds 80%[19,33,36,37].

Survival is directly connected to early diagnosis and periodical revisions, multidisciplinary team, combined therapy, constant clinical tests, services planning and family support[31,34,37,38]. A study with children with acute lymphoid leukemia concluded that those submitted to hematopoietic stem-cell transplant achieved survival compatible with the rates of other European regions[39].

Survival and death by acute lymphoblastic leukemia are related to the age-range with better prognosis for 1-9 years old patients. The data of the current study showed frequency equal to 60.8% for males, 50.2% aged up to 5 years in cases of acute lymphoblastic leukemia and 70.6% originated from Maranhão countryside (70.6%) submitted to chemotherapy alone during treatment (58%) and blood type O (35.9%). Deaths were higher for patients in combined therapy, chemotherapy with radiotherapy (93.8%), suggesting that in these cases, the tumor was more aggressive[40,41].

Similar to the world scenario, this study found that lymphoid leukemia is more prevalent up to 5 years old[38] and because of this diagnosis, the patients are typically prescribed therapeutic modalities as palliative and curative care, the first recommended for incurable tumors or risk of immediate death. Curative care are chemotherapy, radiotherapy and/or surgeries contingent upon the clinical conduct chosen[29,30,37]. These procedures have as main goal to ensure children and adolescents better prognosis and autonomy and increasing survival[37,42].

The most frequent histological types were the cases of lymphoid leukemia followed by myeloid leukemia[17,31]. Patients with lymphoblastic leukemia (UCS) accounted for 54.1% of the cases of death with statistically significant differences compared to other categories of acute lymphoblastic leukemia. These high rates can be associated with late diagnosis because of the existing flaws of public policies[27,29-31].

The lowest death frequency was found in the cases confirmed of precursor B-cells lymphoblastic leukemia[27,29]. It appears that great part of lymphoid leukemias detected was not specified according to their cellular markers potentially leading to several prognosis, what hampers the analysis of death and survival[12,33]. With this in mind, it is believed that the lack of specifications in the patients' charts is a limitation to analyze the cytogenetic aspect. Entering data of the patient in the charts with the required information for better characterization of the cases, follow-up and evolution should be done with care[12,13].

More favorable prognosis of lymphoid leukemia appears not to be related only to the histological type and treatment[43] and that the result of remission or death are very important references. In this perspective, the decline of mortality by cancer concluded by some studies may be associated with new techniques and new chemotherapy protocols with reduced chemotoxicity, allowing potential adaptation and improvement of the prognosis of leukemias[19,24].

CONCLUSION

The findings suggest that most of the patients with lymphoblastic leukemia are up to 5 years males. In addition, it was found that the association between the evolution of the treatment and the histological type of the tumor in patients with acute lymphoblastic leukemia was lower in the cases confirmed of precursor B-cell lymphoblastic leukemia in comparison to other categories. These data indicate that it is necessary to plan measures to promote health and broaden the offer of diagnosis and treatment for cases of hematologic neoplasms.

ACKNOWLEDGMENT

To the Board of HCAB and to Cancer Hospital Registry for authorization and logistics to collect the data.

CONTRIBUTIONS

All the authors contributed substantially to the study design, analysis and interpretation of the data, wording and critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to report.

FUNDING SOURCES

None.

REFERENCES

1. Steliarova-Foucher E, Colombet M, Ries LAG, et al. International incidence of childhood cancer, 2001-10: a population-based registry study. Lancet Oncol. 2017;18(6):719-31. doi: https://doi.org/10.1016/S1470-2045(17)30186-9
2. Bertuccio P, Bosetti C, Malvezzi M, et al. Trends in mortality from leukemia in Europe: an update to 2009 and a projection to 2012. Int J Cancer. 2013;132(2):427-36. doi: https://doi.org/10.1002/ijc.27624
3. Instituto Nacional de Câncer José Alencar Gomes da Silva [Internet]. Rio de Janeiro: INCA; [data desconhecida]. Câncer: tipos de câncer; [modificado 2021 ago 8; acesso 2021 out 19]. Disponível em: https://www.inca.gov.br/tipos-de-cancer
4. Ministério da Saúde (BR), Secretaria de Atenção à Saúde. Protocolos clínicos e diretrizes terapêuticas em oncologia [Internet]. Brasília (DF): Ministério da Saúde; 2014 [acesso 2021 out 19]. Disponível em: http://bvsms.saude.gov.br/bvs/publicacoes/protocolos_clinicos_diretrizes_terapeuticas_oncologia.pdf
5. Campo E, Swerdlow SH, Harris NL, et al. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood. 2011;117(19):5019-32. doi: https://doi.org/10.1182/blood-2011-01-293050
6. Organização Mundial da Saúde. CID-10: Classificação Estatística Internacional de Doenças e problemas relacionados à saúde. São Paulo: Edusp; 2008.
7. Fritz A, Percy C, Jack A, et al., editors. International Classification of Diseases for Oncology (ICD-O). 3rd ed. Geneva: World Health Organization; 2013.
8. Nunes AL. Análise das alterações citogenéticas e sua associação com características clínicas e evolução das crianças e adolescentes com leucemia mieloide aguda [dissertação]. Belo Horizonte (MG): Faculdade de Medicina, Universidade Federal de Minas Gerais; 2016.
9. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. doi: https://doi.org/10.3322/caac.21492
10. Ferlay J, Colombet M, Soerjomataram I, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer. 2019;144(8):1941-53. doi: https://doi.org/10.1002/ijc.31937
11. Presti PF, Macedo CRD, Caran EM, et al. Estudo epidemiológico de câncer na adolescência em centro de referência. Rev Paul Pediatr. 2012;30(2):210-6. doi: https://doi.org/10.1590/S0103-05822012000200009
12. Jemal A, Torre L, Soerjomataram I, et al., editors. The cancer atlas. 3rd ed. Atlanta (GA): American Cancer Society; 2019.
13. Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa 2020: incidência de câncer no Brasil [Internet]. Rio de Janeiro: INCA; 2019 [acesso 2021 out 19]. Disponível em: https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/estimativa-2020-incidencia-de-cancer-no-brasil.pdf
14. World Health Organization. WHO report on cancer: setting priorities, investing wisely and providing care for all [Internet]. Geneva: WHO; 2020 [cited 2020 Mar 7]. Available from: https://apps.who.int/iris/handle/10665/330745
15. Ward ZJ, Yeh JM, Bhakta N, et al. Estimating the total incidence of global childhood cancer: a simulation-based analysis. Lancet Oncol. 2019;20(4):483-93. doi: https://doi.org/10.1016/S1470-2045(18)30909-4
16. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2021. CA Cancer J Clin. 2021;71(1):7-33. doi: https://doi.org/10.3322/caac.21654
17. Churchman ML, Qian M, Te Kronnie G, et al. Germline genetic IKZF1 variation and predisposition to childhood acute lymphoblastic leukemia. Cancer Cell. 2018;33(5):937-48. doi: https://doi.org/10.1016/j.ccell.2018.03.021
18. Sousa DWL, Ferreira FVA, Félix FHC, et al. Acute lymphoblastic leukemia in children and adolescents: prognostic factors and analysis of survival. Rev Bras Hematol Hemoter. 2015;37(4):223-9. doi: https://doi.org/10.1016/j.bjhh.2015.03.009
19. Reis RS, Silva NP, Santos MO, et al. Mother and child characteristics at birth and early age leukemia: a case-cohort population-based study. J Pediatr. 2017;93(6):610-8. doi: https://doi.org/10.1016/j.jped.2016.12.009

20. Cavalcante MS, Santana Rosa IS, Torres F. Leucemia linfoide aguda e seus principais conceitos. Rev FAEMA. 2017;8(2):151-64. doi: https://doi.org/10.31072/rcf.v8i2.578

21. Sossela FR, Zoppas BCA, Weber LP. Leucemia mieloide crônica: aspectos clínicos, diagnóstico e principais alterações observadas no hemograma. Rev Bras An Clin. 2017;49(2):127-30. doi: https://doi.org/10.21877/2448-3877.201700543

22. Chaudhury S, O'Connor C, Cañete A, et al. Age-specific biological and molecular profiling distinguishes paediatric from adult acute myeloid leukaemias. Nat Commun. 2018;9:5280. doi: https://doi.org/10.1038/s41467-018-07584-1

23. Bolouri H, Farrar JE, Triche TJ Jr, et al. The molecular landscape of pediatric acute myeloid leukemia reveals recurrent structural alterations and age-specific mutational interactions. Nat Med. 2018;24(1):103-12. doi: https://doi.org/10.1038/nm.4439

24. Pieters R, Groot-Kruseman H, Van der Velden V, et al. Successful therapy reduction and intensification for childhood acute lymphoblastic leukemia based on minimal residual disease monitoring: study ALL10 from the Dutch Childhood Oncology Group. J Clin Oncol. 2016;34(22):2591-601. doi: https://doi.org/10.1200/JCO.2015.64.6364

25. Pui CH, Yang JJ, Bhakta N, et al. Global efforts toward the cure of childhood acute lymphoblastic leukaemia. Lancet Child Adolesc Health. 2018;2(6):440-54. doi: https://doi.org/10.1016/S2352-4642(18)30066-X

26. Instituto Nacional de Câncer. Registros hospitalares de câncer: planejamento e gestão [Internet]. 2. ed. rev. atual. Rio de Janeiro: INCA; 2010 [acesso 2021 out 19]. Disponível em: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//registros-hospitalares-de-cancer-2010.pdf

27. Ferreira JMO, Klumb CE, Reis RS, et al. Lymphoma subtype incidence rates in children and adolescents: first report from Brazil. Cancer Epidemiol. 2012;36(4):e221-6. doi: https://doi.org/10.1016/j.canep.2012.03.006

28. Kansal R. Classification of acute myeloid leukemia by the revised fourth edition World Health Organization criteria: a retrospective single-institution study with appraisal of the new entities of acute myeloid leukemia with gene mutations in NPM1 and biallelic CEBPA. Hum Pathol. 2019;90:80-96. doi: https://doi.org/10.1016/j.humpath.2019.04.020

29. Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa 2018: incidência de câncer no Brasil [Internet]. Rio de Janeiro: INCA; 2017 [acesso 2021 out 19]. Disponível em: https://portaldeboaspraticas.iff.fiocruz.br/wp-content/uploads/2019/10/estimativa-incidencia-de-cancer-no-brasil-2018.pdf

30. Instituto Nacional do Câncer José Alencar Gomes da Silva. Incidência, mortalidade e morbidade hospitalar por câncer em crianças, adolescentes e adultos jovens no Brasil: informações dos registros de câncer e do sistema de mortalidade [Internet]. Rio de Janeiro: INCA; 2016 [acesso 2021 out 19]. Disponível em: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//incidencia-mortalidade-morbidade-hospitalar-por-cancer.pdf

31. Mutti CF, Cruz VG, Santos LF, et al. Perfil clínico-epidemiológico de crianças e adolescentes com câncer em um serviço de oncologia. Rev Bras Cancerol. 2018;64(3):293-300. doi: https://doi.org/10.32635/2176-9745.RBC.2018v64n3.26

32. Horton TM, Hoff FW, van Dijk A, et al. The effects of sample handling on proteomics assessed by reverse phase protein arrays (RPPA): functional proteomic profiling in leukemia. J Proteomics. 2021;233(1):104046. doi: https://doi.org/10.1016/j.jprot.2020.104046

33. Saraiva DCA, Santos SS, Monteiro GTR. Tendência de mortalidade por leucemias em crianças e adolescentes nas capitais dos estados brasileiros: 1980-2015. Epidemiol Serv Saúde. 2018;27(3):2017310. doi: https://doi.org/10.5123/s1679-49742018000300004

34. Santos MO. Incidência, mortalidade e morbidade hospitalar por câncer em crianças, adolescentes e adultos jovens no Brasil: informações dos registros de câncer e do sistema de mortalidade [resenha de livro]. Rev Bras Cancerol. 2018;64(3):439-40. doi: https://doi.org/10.32635/2176-9745.RBC.2018v64n3.56

35. Feliciano SVM, Santos MO, Pombo-de-Oliveira MS. Incidência e mortalidade por câncer entre crianças e adolescentes: uma revisão narrativa. Rev Bras Cancerol. 2018;64(3):389-96. doi: https://doi.org/10.32635/2176-9745.RBC.2018v64n3.45

36. Kehm RD, Spector LG, Poynter JN, et al. Does socioeconomic status account for racial and ethnic disparities in childhood cancer survival? Cancer. 2018;124(20):4090-7. doi: https://doi.org/10.1002/cncr.31560

37. Iacobucci I, Mullighan CG. Genetic basis of acute lymphoblastic leukemia. J Clin Oncol. 2017;35(9):975-83. doi: https://doi.org/10.1200/JCO.2016.70.7836

38. World Health Organization [Internet]. Geneva: WHO; c2022. Palliative care; 2020 Aug 5 [cited 2019 July 2]. Available from: https://www.who.int/news-room/fact-sheets/detail/palliative-care

39. Kairiene I, Pasauliene R, Lipunova N, et al. Improved outcome of childhood acute myeloid leukemia in an Eastern European country: Lithuanian experience. Eur J Pediatr. 2017;176(10):1329-37. doi: https://doi.org/10.1007/s00431-017-2978-9

40. Nascimento MC. Atendimentos a crianças e adolescentes com câncer em Minas Gerais: retrato de uma década.

Rev Bras Cancerol. 2018;64(3):365-72. doi: https://doi.org/10.32635/2176-9745.RBC.2018v64n3.42

41. Hintz LG, Castro Júnior CG, Lukrafka JL. Perfil clínico-epidemiológico de crianças e adolescentes em tratamento oncológico. Ciênc Saúde. 2019;12(1):31421. doi: https://doi.org/10.15448/1983-652X.2019.1.31421
42. Hrusak O, Haas V, Stancikova J, et al. International cooperative study identifies treatment strategy in childhood ambiguous lineage leukemia. Blood. 2018;132(3):264-76. doi: https://doi.org/10.1182/blood-2017-12-821363
43. Pantoja LC. Estudo da resposta terapêutica e prognóstico de pacientes com diagnóstico de leucemia linfoide aguda com fusões gênicas em um hospital de referência do Pará [dissertação]. Belém (PA): Universidade Federal do Pará; 2018.

Recebido em 14/9/2021
Aprovado em 31/10/2021

Scientific-Editor: Anke Bergmann. Orcid iD: https://orcid.org/0000-0002-1972-8777