Saúde e Pesquisa
DOI: 10.17765/2176-9206.2022v15n3.e10894

Factors associated with the time between diagnosis and initiation of childhood cancer treatment

Fatores associados ao tempo entre o diagnóstico e o início do tratamento do câncer infantojuvenil

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ABSTRACT
This study aimed to analyze the distribution of childhood cancer and identify factors associated with delay in starting cancer treatment, in the state of Paraíba, from the Hospital-Based Cancer Registries (HBCR), from 2010 to 2018. Observational, descriptive and analytical study, with 896 records of children and adolescents (0-19 years), identifying epidemiological and clinical characteristics and compliance with Federal Law 12732/12 (maximum of 60 days to start treatment). Data were analyzed by logistic regression (α=5%). The results showed that 80.2% patients started treatment within the time prescribed by law (≤ 60 days). Individuals aged 10 to 19 years, with solid tumors, undergoing surgery and treated in one of the four HBCR in Paraíba are more likely to have anticancer therapy initiated after 60 days. The delay in starting treatment against childhood cancer is associated with epidemiological and clinical characteristics of pediatric cancer patients.

Keywords: Epidemiology; Hospital; Neoplasm; Pediatrics.

RESUMO
Objetivou-se analisar a distribuição do câncer infantojuvenil e identificar fatores associados ao atraso no início do tratamento oncológico, na Paraíba, a partir dos Registros Hospitalares de Câncer, de 2010 a 2018. Estudo observacional, descritivo e analítico, com 896 registros de crianças e adolescentes (0-19 anos), identificando-se características epidemiológicas, clínicas e o cumprimento da Lei Federal 12.732/12 (lei dos 60 dias para início do tratamento). Os dados foram analisados pela regressão logística (α=5%). Constatou-se que 80,2% dos pacientes iniciaram o tratamento no tempo previsto por lei (≤ 60 dias). Observou-se que indivíduos de 10 a 19 anos, com tumores sólidos, submetidos à cirurgia e tratados em um dos quatro RHC's da Paraíba apresentam maiores chances de terem a terapia antineoplásica iniciada em um tempo superior a 60 dias. Conclui-se que o atraso no início do tratamento contra o câncer infantojuvenil está associado a características epidemiológicas e clínicas dos pacientes oncológicos pediátricos.

Palavras-chave: Epidemiologia. Hospitais. Neoplasias. Pediatria.

Received in February 07, 2022
Accepted on July 03, 2022

INTRODUCTION

Childhood cancer corresponds to a group of several diseases that have in common the uncontrolled proliferation of abnormal cells, which can occur anywhere in the body[1]. Estimates reveal that this type of cancer represents, between 1% and 4%, the incidence of all malignant tumors seen in most populations. In Brazil, its representativeness corresponds to the first cause of death (8% of the total) from disease among children and adolescents[2].

It is important to emphasize that childhood cancer is not a preventable disease. Although some types of cancer in children and adolescents may be associated with environmental factors, early diagnosis is essential, in order to provide children and adolescents with quality anticancer treatment and a greater probability of cure[2].

On the other hand, late diagnosis has a negative impact on the course of treatment that the patient will undergo, as well as on the mortality and survival of these patients, which may be related to the need for specialized care, the lack of access to a medical service and to accurate exams that can help and avoid future delays[3-5].

Therefore, it is necessary to raise awareness of the health system for the early diagnosis of cancer in children and adolescents. Therefore, the team of health professionals that works at different points in the Brazilian Health Care Network (RAS - *Rede de Atenção à Saúde*) for children and adolescents with cancer must be prepared to identify children and adolescents with suspicious signs and symptoms and to refer these patients to other levels of care, with the aim of investigating suspected cases, aiming at diagnostic confirmation and rapid initiation of cancer treatment[6-8].

Considering that Primary Health Care (PHC) is the level of assistance in which the first contact with the health system is made, the effective performance of this level of care in the monitoring, surveillance and promotion of the health of children and adolescents is strategic, enabling early detection of signs and symptoms of cancer[6.7].

In this sense, initiatives involving professionals working in PHC, promoting learning capable of improving this scenario, are being instituted and have shown to be effective in the detection of children and adolescents with suspected cancer, as well as in reducing the time, from the perception of signs and symptoms to the arrival of these patients to referral centers[6].

In addition to the difficulties in obtaining an accurate diagnosis, due to the centralization of quality treatments in the capitals, the lack of access impairs patients who need to travel, from the first consultation to the beginning of treatment, with the delay or withdrawal due to lack of resources[9].

Thus, the analysis of records of care provided at the hospital level can provide relevant information about the health care offered to pediatric cancer patients at this

level of care, enabling improvements in their administrative and care processes[10].

From this perspective, Hospital-Based Cancer Registry (HBCR) are sources installed in general or specialized oncology hospitals, acting as collection centers that allow, from their information, to monitor the care provided to the patient, in order to collect data regarding the diagnosis, treatment and evolution of cases of malignant neoplasms treated in institutions (public, private, philanthropic or university). Such information is sent to compose the national base of cancer hospital records, kept by INCA, from the Integrator HBCR[10].

In Brazil, according to Federal Law 12732/2012, patients with a confirmed diagnosis of cancer must have anticancer treatment instituted within 60 days from the date of signature of the pathology report[11]. Most patients undergo treatment within this period, however there is still a percentage of pediatric cancer patients who start treatment after this period[12].

In this context, it is worth to emphasize that Paraíba is the state in the Northeast region with the highest number of new cases of childhood cancer expected in the triennium 2020-2022 and that the number of estimated cases exceeds the average for the Northeast region and the average for Brazil[2].

Therefore, the objective of the present study was to analyze the distribution of childhood cancer and identify factors associated with the time between diagnosis and initiation of treatment in the state of Paraíba, based on the Hospital-Based Cancer Registry (HBCR), in the period from 2010 to 2018.

METHODOLOGY

STUDY TYPE AND ETHICAL CONSIDERATIONS

This was an observational, analytical, retrospective study, based on secondary records. This research does not require the Ethics Committee approval, as it was carried out with secondary data integrated in the Brazilian Hospital-Based Cancer Registries System, which are made available by the National Cancer Institute (INCA), making them freely accessible.

POPULATION AND SAMPLE

The study population consisted of all patients aged 0 to 19 years (n=937), residing in the state of Paraíba, who were included in the Health Information System of the Brazilian Hospital-Based Cancer Registries System, available in the Integrator Module of Hospital-Based Cancer Registries, from 2010 to 2018.

The sample comprised patients in the age group of interest (0 to 19 years), of both genders, in attendance at one of the four HBCR in the state of Paraíba, from 2010 to 2018. Records of patients classified as non-analytical cases were excluded, in order to avoid double entry and, consequently, data overestimation.

Analytical cases are those whose treatment planning and institution were carried out in the same hospital (HBCR), as well as monitoring the evolution of the disease and the patient's quality of life. These cases are suitable for analyzing the quality of care provided to cancer patients[10].

DATA COLLECTION

Data were collected using the Integrator Module for Hospital-Based Cancer Registry, and the explanatory variables of interest were classified into sociodemographic variables (gender, age, skin color and number of the National Registry of Healthcare Establishments/ hospital CNES) and clinical and treatment variables (date of first consultation, date of first diagnosis, type of tumor, date of initiation of the first treatment at the hospital), as seen in Box 1.

As a dependent variable, the time to start the treatment was analyzed. For this purpose, the time interval (in days) between the date of diagnosis and the start the treatment of pediatric cancer patients was calculated to verify whether the state of Paraíba is complying with Law 12732/2012.

Box 1. Dictionary of dependent variables analyzed in the study

Variables	Categories
Gender	Male Female
Age group	0 to 4 years 5 to 9 years 10 to 14 years 15 to 19 years
Skin color	White Black Yellow Brown Indigenous
Date of diagnosis	dd/mm/yyyy
Date of start of treatment	dd/mm/yyyy
Type of neoplasm	Solid tumor Hematologic neoplasm
Type of treatment	None Surgery Radiotherapy Chemotherapy Hormone therapy Bone marrow transplant Immunotherapy Others
Treatment hospital	Hospital Napoleão Laureano Hospital Alcides Carneiro Hospital da Fundação Assistencial da Paraíba Hospital São Vicente de Paulo

The dependent variable corresponded to the time to start treatment, which was categorized into intervals ≤ to 60 days and > to 60 days.

DATA ANALYSIS

Data obtained were tabulated and processed in a Microsoft Excel™ spreadsheet. An exploratory analysis was performed, and then Pearson's chi-square test was applied to check for associations between the variables, assessing whether the observed proportions show significant differences or not. After, the logistic regression method was used, analyzing the time between diagnosis and the start of cancer treatment (≤ 60 days or > 60 days) and the independent variables: gender, age group, skin color, type of neoplasm, type of treatment and hospital. Thus, the odds ratio (OR) identified the patient's chances of undergoing treatment within the period established by law, based on independent variables, adopting the p-value of 0.05.

Variables with p-values lower than 0.30 were included in the logistic regression and, in the final model, those with p-values 0.05 were retained. Logistic regression allowed the generation of a logistic model capable of predicting the probability of an individual with childhood cancer starting their treatment in a time less than or equal to 60 days, according to the variables associated with the outcome, such as age group, type of treatment and the hospital in which the patient received the treatment.

Regarding the variables associated with the outcome, the odds ratio (OR) and confidence interval (95%) were calculated to identify, for each variable, the probability of a child or adolescent with childhood cancer starting their oncological treatment within a period of time greater than 60 days.

The final model was evaluated through the values of accuracy, sensitivity, specificity and by the deviance function (D). A tool used to check the quality of fit of the final model was the receiver operating characteristic (ROC) curve, obtained from the graph of sensitivity versus the false positive rate (1-Specificity) or complement of specificity.

Therefore, in order to estimate the probability of identifying which individuals underwent cancer treatment in a time ≤ 60 days or > 60 days, a decision rule was adopted that was based on the cut-off point, in which the probability was summarized in a dichotomous answer. Patients who obtained an estimated probability below or above the cut-off point were classified, respectively, as those who underwent treatment within a period of less than or equal to 60 days, in a period of more than 60 days. The analyses were run in the RStudio software version 4.1.0.

RESULTS

The records of the 896 children and adolescents assisted at the 4 HBCR in the state of Paraíba showed that the mean age of the patients was 9.84 years (±6.09) and a median of 10 years; 52.7% (n=472) were male, and 30.8% (n=276) were aged between 15 and 19 years. Regarding skin color, 67.7% (n= 606) declared themselves to be brown; 57.3% (n=513) had solid neoplasia; 67.3% (n=603) patients were

treated at Napoleão Laureano Hospital, and 80.2% (n=719) performed the procedures within the time prescribed by law (≤ 60 days), as seen in Table 1.

Table 1. Distribution of the number of cases of childhood cancer, according to gender, age group, skin color, type of neoplasm and time interval between diagnosis and start of treatment, Paraíba, Brazil, 2010–2018

Variables		Absolute Frequency (n)	Relative Frequency (%)
Gender	Male	472	52.7
	Female	424	47.3
	Total	896	100
Age group (a years)	0 to 4	251	28.0
	5 to 9	168	18.8
	10 to 14	201	22.4
	15 to 19	276	30.8
	Total	896	100
Skin color	White	209	23.3
	Brown	606	67.7
	Black	12	1.3
	Indigenous	03	0.3
	Yellow	05	0.6
	No information	61	6.8
	Total	896	100
Type of neoplasm	Solid	513	57.3
	Hematologic	383	42.7
	Total	896	100
Type of treatment	Chemotherapy	356	39.7
	Surgery	102	11.4
	Radiotherapy	87	9.7
	Bone marrow transplant	00	00
	Hormone therapy	01	0.1
	Immunotherapy	00	00
	Others	96	10.7
	No information	254	28.4
	Total	896	100
Treatment hospital	Napoleão Laureano Hospital	603	67.3
	Alcides Carneiro Hospital	189	21.1
	Fundação Assistencial da Paraíba Hospital	89	9.9
	São Vicente de Paulo Hospital	15	1.7
	Total	896	100
Time	≤ 60 days	719	80.2
	> 60 days	177	19.8
	Total	896	100

Source: INCA HBCR worksheets from 2010 to 2018, accessed on April 15, 2020.

As for the time to start treatment, 89.2% (n=130) patients aged 0 to 4 years underwent treatment in less than 60 days and 25.4% (n=70) patients aged 15 to 19 years underwent treatment for more than 60 days. When testing the association between the independent variables of the study and the time interval for the start of treatment, the variables "age group", "skin color", "type of neoplasm", "type of treatment" and "treatment hospital" proved to be significant (Table 2).

Table 2. Bivariate analysis of the association between epidemiological and clinical variables and the time interval between diagnosis and start of treatment, Paraíba, Brazil, 2010–2018

Variables		Time interval between diagnosis and start of treatment						p-value
		≤ 60 days		> 60 days		Total		
		n	%	n	%	n	%	
Gender	Male	380	80.5	92	19.5	472	100	**0.9009**
	Female	339	79.9	85	20.1	424	100	
Age group (years)	0 to 4	224	89.2	27	10.8	251	100	**0.0002***
	5 to 9	130	77.4	38	22.6	168	100	
	10 to 14	159	79.1	42	20.9	201	100	
	15 to 19	206	74.6	70	25.4	276	100	
Skin color (1)	White	160	76.6	49	23.4	209	100	**0.14***
	Black	11	91.7	001	8.3	12	100	
	Yellow	05	100	00	00	05	100	
	Brown	496	81.8	110	18.2	606	100	
	Indigenous	02	66.7	01	33.3	03	100	
Type of neoplasm	Solid	403	78.6	110	21.4	513	100	**0.1664***
	Hematologic	316	82.5	67	17.5	383	100	
Type of treatment (2)	Chemotherapy	309	86.8	47	13.2	356	100	**<0.0001***
	Radiotherapy	32	36.8	55	63.2	87	100	
	Surgery	81	79.4	21	20.6	102	100	
	Bone marrow transplant	00	00	00	00	00	00	
	Hormone therapy	01	100	00	00	01	100	
	Immunotherapy	00	00	00	00	00	00	
	Others	78	81.2	18	18.8	96	100	
	No information	218	85.8	36	14.2	254	100	
Treatment Hospital	Napoleão Laureano Hospital	512	84.9	91	15.1	603	100	**<0.0001***
	Alcides Carneiro Hospital	161	85.2	28	14.8	189	100	
	FAP Hospital	32	35.9	57	64.1	89	100	
	São Vicente de Paulo Hospital	14	93.3	01	6.7	15	100	

Source: INCA HBCR worksheets from 2010 to 2018, accessed on April 15, 2020.
* Variables with p-value<0.30.
(1) To test the association, the "Black/Indigenous/Yellow" categories were pooled.
(2) To test the association, the categories "BMT/Hormone Therapy/Immunotherapy/Others" were pooled.

As seen in Table 3, pediatric cancer patients aged 10 to 14 years and 15 to 19 years were, respectively, 1.76 times and 1.77 times more likely to start cancer treatment in a time greater than 60 days, when compared those aged 0 to 9 years. Regarding the type of treatment, children and adolescents undergoing chemotherapy were 2.54 times less likely to start cancer treatment in a period longer than 60 days, compared to those undergoing surgery, radiotherapy and other types of treatment.

When considering the HBCR in which the pediatric oncology patient was assisted, children and adolescents who underwent treatment at Napoleão Laureano Hospital were 7.63 times less likely to start treatment in a period of more than 60 days compared to those assisted at the FAP Hospital. Additionally, pediatric cancer patients who underwent treatment at São Vicente de Paulo Hospital and Alcides Carneiro Hospital had, respectively, 13.13 and 4.89 less chances of starting their treatment in a period of more than 60 days, compared to those who received treatment at the FAP Hospital.

Table 3. Variables associated with the time recommended by law for starting cancer treatment in children and adolescents, Paraíba, Brazil, 2010–2018

Variable	Parameter Estimates	Standard error	*p-value	Odds Ratio	95% CI
Age group from 10 to 14 years	0.5673	0.2686	0.034680*	1.7635349	1.041704890; 2.9855439
Age group from 15 to 19 years	0.5700	0.2461	0.020531*	1.7683490	1.091700718; 2.8643916
Chemotherapy	-0.9336	0.2545	0.000245*	0.3931525	0.238723607; 0.6474806
Napoleão Laureano Hospital	-2.0331	0.2829	6.67e-13*	0.1309281	0.075198152; 0.2279601
São Vicente de Paulo Hospital	-2.5752	1.0867	0.017801*	0.0761360	0.009048392; 0.6406323
Alcides Carneiro Hospital	-1.5879	0.3683	1.62e-05*	0.2043459	0.099274071; 0.4206259

*p-valor < 0.05
Reference category for the age group variable: 0 to 9 years old; Reference category for the treatment variable: Surgery, Radiotherapy and Other types of treatment; Reference category for HBCR: Fundação Assistencial da Paraíba Hospital.
Source: INCA HBCR worksheets from 2010 to 2018, accessed on April 15, 2020.

The validity of the adjusted model was verified from deviance. Thus, the calculation of the deviation function (576.1595) for the model that was fitted was lower than the value found in the Chi-square reference (694.7326), indicating that the model is statistically accepted, as it complies with the required criteria.

Figure 1 illustrates the ROC curve constructed for the model in Paraíba. The values for the cut-off point were 0.180, sensitivity of 64.5%, specificity of 70.9%, area under the curve equal to 74.5% and accuracy of 69.47%.

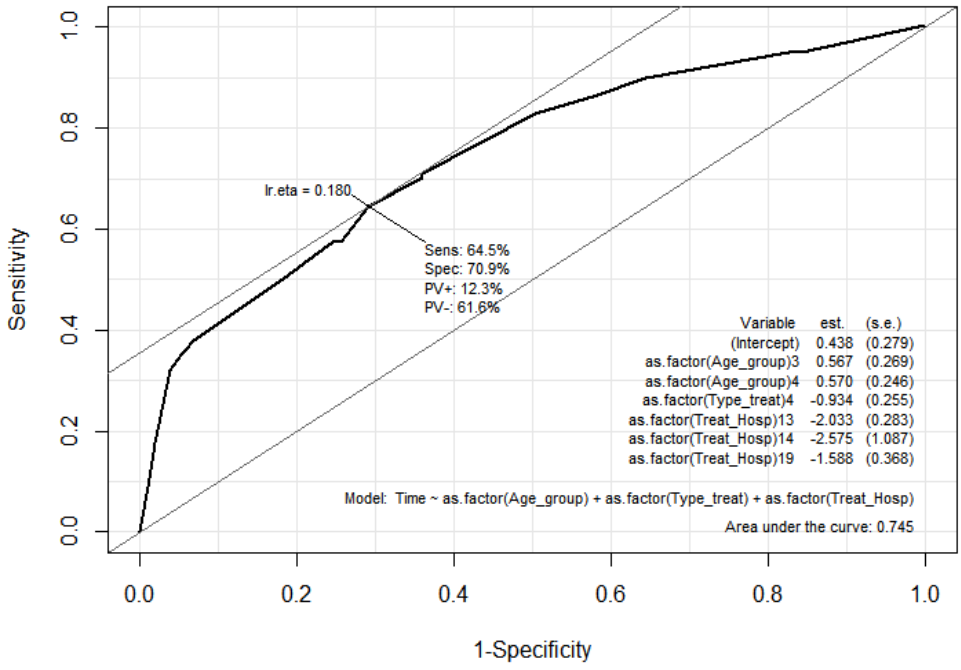

Figure 1. ROC curve for the logistic regression model.
Source: INCA HBCR worksheets from 2010 to 2018, accessed on April 15, 2020.

For the analyzed time series, the present study also revealed delays, with the highest percentage in 2015 (26.8%) and the lowest in 2016 (10.9%) of children and adolescents assisted in Paraíba who started treatment more than 60 days after diagnosis, as seen in Figure 2.

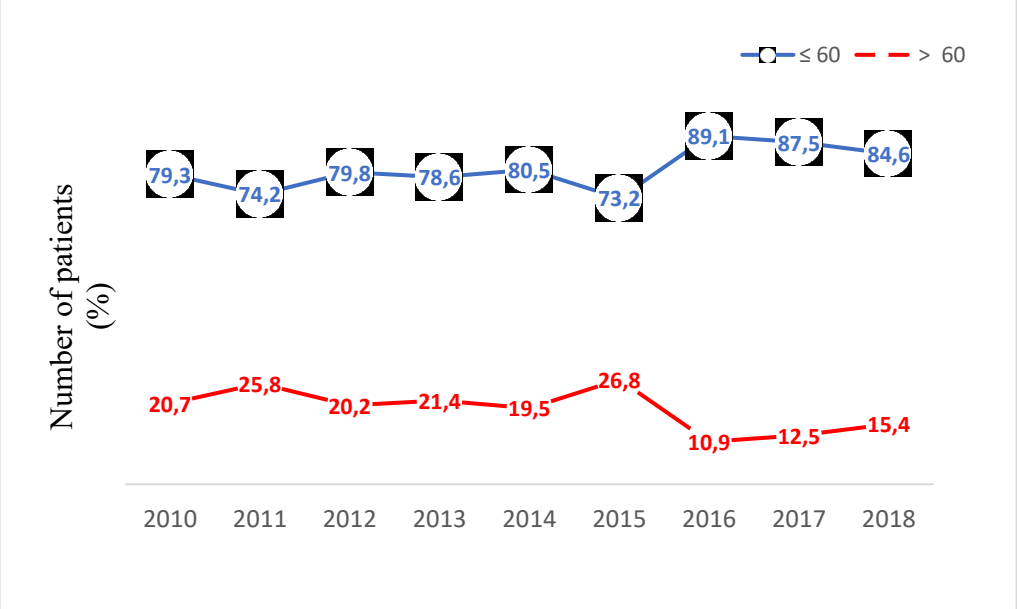

Figure 2. Annual distribution, in percentage values, of pediatric cancer patients according to the start of treatment within the time recommended by law, Paraíba, Brazil, 2010 - 2018
Source: INCA HBCR worksheets from 2010 to 2018, accessed on April 15, 2020.

DISCUSSION

In the present study, the characterization of the distribution of childhood cancer in the state of Paraíba, from 2010 to 2018, allowed to analyze the time between diagnosis and the start of cancer treatment. This information is relevant, considering that the delay in starting treatment can decrease the cure rate or survival rate of pediatric cancer patients[13]. Studies analyzing the time between diagnosis and the start of cancer treatment make it possible to check compliance with Law 12732 and identify whether, since the creation of this legal rule, there has been an increase in records of children and adolescents who started cancer treatment in the public health network, within up to 60 days, from the diagnosis.

In this sense, our results allowed a better understanding of the care offered to children and adolescents with cancer, noting that an expressive percentage of these patients started cancer treatment after the period prescribed by law and that such delay was related to epidemiological and clinical characteristics.

Regarding the epidemiological aspects, in this study, there was a higher frequency of childhood cancer records in males, corroborating national[12,14,15] and

international[16,17] studies. One hypothesis for these findings is that male individuals may be more exposed to risk factors[18], presenting a greater possibility of congenital diseases, conditions that would increase the risk of childhood cancer[19].

As for the age group, in the present study, records of patients aged between 15 and 19 years predominated. These findings differ from other studies carried out in Brazil that identified a higher frequency of childhood cancer in children aged 0 to 4 years[12,14]. A possible explanation for our results is that, in Paraíba, the percentage of the population aged between 15 and 19 is higher than that observed in Brazil[20].

In relation to skin color, according to the Brazilian National Institute of Geography and Statistics (IBGE) census, in 2010[20], 50.7% Brazilians classified themselves as black or brown, becoming the majority in Brazil. This scenario would justify the findings of the present study and other studies carried out in Brazil, which found a higher percentage of brown-skinned children and adolescents affected by childhood cancer[12,21,22].

In this study, solid tumors were more frequently observed, and these results are corroborated by other studies carried out in Brazil[12,23]. Regarding this finding, analysis of temporal trends in childhood cancer recorded a significant increase in the prevalence rates of solid tumors from 2000 to 2018, with variations between Brazilian regions[24].

With respect to the type of treatment, chemotherapy was the most used therapeutic modality in pediatric cancer patients, as observed in other studies[12,25]. In fact, chemotherapy is the approach most commonly instituted as the first treatment against various types of cancer in children and adolescents[26,27], with the objective of eradicating cancer, preventing its recurrence and achieving long-term control of the disease[27], with high cure rates provided by chemotherapy protocols in hematological neoplasms[28] and solid tumors[29].

As for the greater number of hospital records observed at the Napoleão Laureano Hospital, this can be justified by the fact that it is a reference for cancer treatment in Paraíba, being the only one among the four HBCR analyzed, considered by the Ministry of Health as a Center of High Complexity Cancer Assistance (CACON - *Centro de Assistência de Alta Complexidade em Oncologia*) with a pediatric unit[1].

From this perspective, the creation, in the 1990s, of a regionalized and hierarchical network of oncology care centers that provide assistance through the Unified Health System[30,31] favored the expansion of access and comprehensive care to cancer patients. In the present study, the 4 HBCR in Paraíba, despite having different legal natures (philanthropic entity, public or private), have their patients mostly assisted by the SUS, reinforcing the importance of the SUS in cancer care.

The current oncology care policy was structured in the logic of the Health Care Networks (RASs) in the SUS, aiming

to improve the quality of life of users, reduce mortality, incidence and disabling conditions caused by cancer, through actions of promotion, prevention, early detection, timely treatment and palliative care[32]. However, in order to provide comprehensive care to pediatric cancer patients, aiming at health promotion and health care, collaborative teamwork and the establishment of permanent communication between all the different points of the RAS are essential[8,33].

Regarding compliance with Federal Law 12732[8], in the present study, 80.2% patients underwent treatment in a time less than or equal to 60 days. The fact that 19.8% children and adolescents in Paraíba do not start anticancer treatment within 60 days, as established by law, is worrisome. Considering the peculiarities of childhood cancer, particularly, with shorter latency periods, rapid growth and very invasive[7], it has even been suggested to reduce the maximum time to start treatment recommended by the Law of 60 days for this group of patients[13]. Reinforcing this concern, in Brazil, from 1996 to 2017, approximately 42% children aged 0 to 4 years old died from different types of cancer, indicating the need for strategies that favor better access for these patients to the health system[34].

Our findings reinforce that information obtained through the HBCR can support health promotion actions, at an individual and collective level. Since, in Brazil, the coordination of health care is primarily carried out by the PHC, the continuous monitoring of families and the bonds established between the team of professionals who work at this level of care and the population favor the suspicion/identification of the first signs and symptoms of childhood cancer, as well as, when necessary, referral of children and adolescents to specialized centers.

From this perspective, it is essential to identify factors associated with delays in starting cancer treatment in children and adolescents. In the present study, patients aged 10 to 14 and 15 to 19 years old were more likely to have anticancer therapy started in a period of more than 60 days compared to younger patients. These findings are corroborated by Moreira et al. (2021)[12], who, based on data from Brazilian HBCR from 2010 to 2016, found that the time to start treatment in children aged 0 to 4 years was less than 60 days, corresponding to 89% cases and only 76% patients aged 15 to 19 years had started treatment before 60 days.

Similar results were found in Nigeria, a country in which patients younger than 5 years old had a shorter delay in starting treatment compared to those in other age groups[35]. For these authors, such findings could be attributed to the fact that the most frequent tumors in this age group are aggressive and the possibility that they manifest clinically more quickly, favoring a faster diagnosis, as well as the institution of adequate treatment. Another hypothesis would be the higher frequency of consultations recommended for children in

the first years of life[36], favoring continuous follow-up.

Importantly, adolescence is a period of transition in the life of a young person, being surrounded by several changes and uncertainties. When a teenager is faced with the possibility of having cancer, the search process for investigation and definition of the diagnosis is quite time consuming. The necessity of several tests and the drastic change in the routine generate interruptions in plans for their independence, leaving the teenager quite fearful about what is happening[37]. Thus, the chances of an adolescent delaying treatment are greater, and it is important to emphasize that early diagnosis and rapid initiation of treatment are decisive for this age group. In addition, adolescents are often assisted in health services intended for adults and not accompanied by specialists in pediatric oncology, neglecting the specificities that would need to be considered in the management of these patients[38].

A study carried out in the state of Paraná identified that adolescents (10 to 19 years old) had an approximately three times greater risk of death, compared to that observed in children[39]. Therefore, the findings of the present study are worrisome, which showed that adolescents from Paraíba are more likely to have treatment started after 60 days, compared to younger children.

Regarding the type of treatment, the institution of chemotherapy as the first therapeutic resource decreased by 2.54 the probability of the patient undergoing treatment in a time greater than 60 days in relation to surgery, radiotherapy and other types of treatment. These findings can be explained by the greater complexity of surgical procedures compared to chemotherapy, as problems such as cancellation of surgeries after hospitalization, risks of hospital infection, reduced availability of beds are found in the daily routine of hospital care[40].

Considering the HBCR in Paraíba that provide care to pediatric cancer patients, in one of them, there are difficulties in instituting cancer treatment within the time recommended by law, when compared to the other three HBCR. These findings could be explained by weaknesses in the provision of comprehensive and continued care to patients who need different treatment modalities in that HBCR. In this perspective, studies developed to evaluate cancer care offered to patients with other types of cancer point out that characteristics of the health system related to its organization and capacity contribute to delay the beginning of cancer treatment, such as the deficit in the offer of radiotherapy treatment[41,42].

Some aspects related to cancer care for children and adolescents deserve to be highlighted. One of them is the flow of trips by children and adolescents with cancer in the North and Northeast regions, since cancer care networks are located around the capitals, making these users need to travel to carry out the treatment. In order to undergo chemotherapy or radiotherapy, about 58% patients had to travel more than

1,000 km to reach the unit that would offer these therapeutic modalities[9].

Thus, although the patient is often able to access cancer treatment, according to the location and region where it is provided, there may be differences that impact the health services offered and cause a delay in the time prescribed by law, placing the institution of treatments below the standard recommended by the Ministry of Health[43].

Recent studies carried out in Brazil on the time between diagnosis and initiation of treatment for childhood cancer point to regional inequalities in the provision of pediatric cancer care, identifying more significant delays in the North and Northeast regions[12,24]. From this perspective, it is important and strategic to analyze, at the local level, compliance with Law 12732 and to better understand the scenario of pediatric cancer patients from the state of Paraíba. Therefore, our findings are worrisome when identifying such delays.

Although, in this study, patients with solid tumors started cancer treatment more than 60 days later, the type of tumor was not associated with such delay. As for these findings, studies indicate that oncopediatric patients diagnosed with solid tumors are more often delayed in instituting antineoplastic treatment compared to those with hematological malignancies[12,13,24], corroborating our results.

These results could be explained by the fact that the first treatment modality recommended for solid tumors is, more commonly, radiotherapy and surgery, compared to hematological neoplasms, for which chemotherapy is the most widely used first therapeutic resource[26,27]. In this logic, children and adolescents may need to be referred to other specialized centers to receive radiotherapy[14] and/or undergo surgery[40], which could explain a longer time to start treatment when these therapeutic modalities are indicated.

This study has limitations that include the possibility of information and selection bias, since it analyzed data obtained from a secondary database, in addition to the imprecision of the records contained therein due to incomplete information for some variables evaluated.

Nevertheless, it was possible to identify factors associated with the delay in starting cancer treatment in children and adolescents, and this information is essential to understand weaknesses in the provision of cancer care and to favor the search for comprehensive care for pediatric cancer patients.

From this perspective, the results of the present study reveal that continuing health education processes should be encouraged for professional qualification in the Health Care Network for children and adolescents with cancer, with emphasis on PHC teams, for early suspicion and the establishment of agile and resolute flows of childhood cancer. Our results also indicate that special attention should be directed to adolescents with suspicious signs and symptoms, to pediatric cancer patients who need to undergo surgery and to those who

are not undergoing treatment at a Center of High Complexity Cancer Assistance (CACON) with a pediatric unit, as they are more likely to have anticancer treatment instituted within a period of more than 60 days.

Therefore, these findings reinforce the need to build an articulated cancer care network that favors comprehensive care with an adequate supply of services and that considers the particularities of diagnostic and therapeutic interventions aimed at childhood cancer.

CONCLUSIONS

Among the pediatric cancer patients in the Hospital-Based Cancer Registry (HBRC) system of the state of Paraíba, from 2010 to 2018, male children and adolescents predominated, aged between 15 and 19 years, with a median age of 10 years, with brown skin, diagnosed with solid neoplasm, undergoing chemotherapy and treated at Napoleão Laureano Hospital.

Most children and adolescents underwent cancer treatment in a time interval less than or equal to 60 days, as established by Law 12732. However, pediatric cancer patients aged 10 to 19 years, with solid tumors, undergoing surgery and treated in one of the four HBRC in the state of Paraíba are more likely to have anticancer therapy initiated in a time period greater than 60 days.

These findings demonstrate that epidemiological and clinical characteristics of pediatric cancer patients influence the time to start cancer treatment.

ACKNOWLEDGEMENTS

To the National Council for Scientific and Technological Development, for granting an undergraduate scholarship (CNPq - Process 129111/2020-1) and to the Paraíba State Research Support Foundation, for granting a doctoral grant (FAPESQ - Term 010/19, Process 23038. 004264/2015-03).

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