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Epidemiology in pediatric patients with leukemia in a reference hospital in Paraíba Epidemiologia em pacientes pediátricos com leucemia em um hospital de referência

Epidemiología en pacientes pediátricos con leucemia en un hospital de referencia en Paraíba

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#### **ABSTRACT**

na Paraíba

Objective: To analyze the epidemiological profile of children and adolescents diagnosed with leukemia at an oncology center in the capital of Paraíba. Method: Observational, documentary, descriptive, and retrospective study, through the evaluation of medical records of 83 pediatric patients diagnosed with leukemia between May 2018 and May 2023, at the philanthropic hospital Napoleão Laureano, Paraíba. Anthropometric data, family history, treatment, and outcome were collected. The research site was chosen due to high demand and its location as a reference center. Data were collected using a structured form for statistical analysis of absolute and relative frequencies, in addition to the application of the chi-square test and Fisher's exact test for bivariate analysis. The results were presented in tables and graphs. Results: The average age range was 6.5 years, with a higher incidence in preschool children (44.58%). There was a greater predominance of females (53%) and mixed race (91.6%). Macroregion 1 had the highest number of patients (73.5%). The most prevalent symptoms were fever (66.26%), bleeding, bruising, and petechiae (34.93%). Acute lymphoblastic leukemia was the most common type (74.7%), including among deaths (68.2%). Chemotherapy was the most commonly used treatment (88%). Conclusion: The study revealed information about the epidemiological profile of the pediatric leukemia population in Paraíba. Despite the high potential for cure, mortality was high compared to developed countries, possibly resulting from limited access and socioeconomic factors. Therefore, improving information recording, as well as early detection, are essential actions, in addition to encouraging professional training strategies and investment in treatments.

Descriptors: Childhood leukemia; Pediatric epidemiology; Inequality in access to oncological health.

#### **RESUMO**

Objetivo: Analisar o perfil epidemiológico do público infantojuvenil diagnosticado com leucemia em centro oncológico na capital paraibana. Método: Estudo observacional, documental, descritivo e retrospectivo, por meio da avaliação dos prontuários de 83 pacientes pediátricos, diagnosticados com leucemia, entre maio de 2018 e maio de 2023, no hospital filantrópico Napoleão Laureano, Paraíba. Foram coletados dados antropométricos, histórico familiar, tratamento e desfecho. O local de pesquisa foi escolhido devido à alta demanda e ser polo de referência. Os dados foram coletados por meio de ficha estruturada para investigação estatística das frequências absolutas e relativas, além da aplicação dos testes Quiquadrado e teste exato de Fisher para análise bivariada. A apresentação dos resultados foi feita em tabelas e gráficos. Resultados: A faixa etária média foi de 6,5 anos, com maior incidência



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em crianças pré-escolares (44,58%). Houve maior predomínio do sexo feminino (53%) e etnia parda (91,6%). A macrorregião macro 1 teve o maior número de pacientes (73,5%). Os sintomas mais prevalentes foram febre (66,26%), sangramentos, hematomas e petéquias (34,93). A leucemia linfoblástica aguda foi o tipo mais comum (74,7%), inclusive entre os óbitos(68,2%). A quimioterapia foi o tratamento mais usado (88%). **Conclusão:** O estudo revelou informações sobre o perfil epidemiológico do público pediátrico de leucemia na Paraíba. Apesar do alto potencial de cura, a mortalidade foi alta comparada a países desenvolvidos, possivelmente resultada de limitações de acesso e fatores socioeconômicos. Logo, aprimorar o registro das informações, assim como detecção precoce, são ações essenciais, além do incentivo em estratégias na capacitação profissional e investimento em tratamentos.

Descritores: Leucemia infantil: Epidemiologia pediátrica: Desigualdade no acesso à saúde oncológica.

#### RESUMEN

Objetivo: Analizar el perfil epidemiológico de la población infantojuvenil diagnosticada con leucemia en un centro oncológico de la capital paraibana. **Método:** Estudio observacional, documental, descriptivo y retrospectivo, mediante la evaluación de las historias clínicas de 83 pacientes pediátricos diagnosticados con leucemia entre mayo de 2018 y mayo de 2023, en el hospital filantrópico Napoleão Laureano, en el estado de Paraíba. Se recolectaron datos antropométricos, antecedentes familiares, tipo de tratamiento y desenlace clínico. El lugar de investigación fue seleccionado por su alta demanda y por ser un centro de referencia. La recolección de datos se realizó a través de un formulario estructurado para análisis estadístico de frecuencias absolutas y relativas, además de la aplicación de la prueba de Chi-cuadrado y la prueba exacta de Fisher para el análisis bivariado. La presentación de los resultados se efectuó mediante tablas y gráficos. Resultados: La edad promedio fue de 6,5 años, con mayor incidencia en niños en edad preescolar (44,58%). Se observó un predominio del sexo femenino (53%) y de la etnia mestiza (91,6%). La macrorregión 1 presentó el mayor número de pacientes (73,5%). Los síntomas más prevalentes fueron fiebre (66,26%) y sangrados, hematomas y petequias (34,93%). La leucemia linfoblástica aguda fue el tipo más frecuente (74,7%), incluso entre los fallecimientos (68,2%). La quimioterapia fue el tratamiento más utilizado (88%). Conclusión: El estudio reveló información relevante sobre el perfil epidemiológico de la población pediátrica con leucemia en el estado de Paraíba. A pesar del alto potencial de curación, la mortalidad fue elevada en comparación con países desarrollados, posiblemente debido a limitaciones en el acceso a los servicios de salud y a factores socioeconómicos. Por lo tanto, mejorar el registro de datos clínicos, así como la detección precoz, son acciones esenciales, además de fomentar estrategias de capacitación profesional e inversión en tratamientos.

Descriptores: Leucemia infantil; Epidemiología pediátrica; Desigualdad en el acceso a la atención oncológica.

#### INTRODUCTION

Cancer is the second leading cause of mortality in the pediatric population in developed countries and third in underdeveloped countries, according to data from 2019<sup>(1)</sup>. Among these malignant neoplasms, leukemia is the most common disease in children, with a proportion of approximately 30% of all cancers diagnosed before the age of 15<sup>(1)</sup>.

Despite advances in the management of pediatric leukemia, as well as early detection, challenges persist, especially in less favored regions, such as the Northeast of Brazil, particularly in Paraíba, where there is a high mortality rate, around 26.5%. In addition, the complexity and costs associated with treatment highlight the urgency of actions that integrate public health and its promotion, focusing on the appropriate prevention, diagnosis, and follow-up.

In this context, leukemia, the principal cause of death by pediatric cancer, represents a real obstacle to public health<sup>(2)</sup>. It is noteworthy that the pathology affects the production of blood cells responsible for defending the body. Symptoms may vary depending on the type and stage of the disease and include asthenia, fever, bleeding, bruising, petechiae, abdominal distension and/or pain, arthralgia, lymph node enlargement, weight loss or appetite loss<sup>(3)</sup>.

Therefore, given the clinical richness of the pathology, the research carried out at the Napoleão Laureano Hospital, in João Pessoa, Paraíba, is justified, considering the importance of knowing the reality of diagnosed children and adolescents from Paraíba, as well as the scientific, legislative and social efforts to reduce mortality and increase the quality of life of individuals.

Hematological neoplasia is a serious disease, but with proper support, it has a good chance of being cured, approaching 90% when diagnosed early<sup>(4)</sup>. The prognosis varies depending on the type, age, and treatment. According to the literature, there are more than 12 types, with acute leukemia standing out and accounting for approximately 95% of childhood leukemias<sup>(5)</sup>.

The risk of acute lymphoblastic leukemia (ALL) is even higher in children under five years of age and slowly decreases until age 20, then increases again after age 50. It is worth noting that chronic forms are rarer in childhood (5).

According to the Estimate of Cancer Incidence in Brazil, prepared by the National Cancer Institute (INCA) for

the three years 2023-2025, without considering non-melanoma skin tumors, leukemia ranks tenth among the most common cancers in Brazil. Sixth place is observed only in the Northeast region of the country<sup>(2)</sup>.

Furthermore, according to data presented by INCA, in 2022, the incidence of hematological neoplasia in Paraíba was 240 new cases per 100,000 inhabitants, with 60 of these new diagnoses in João Pessoa, the state capital<sup>(2)</sup>.

New legislative updates in Brazil were created to offer better care for the pediatric population, such as Law 14,308/2022, which encouraged scientific research in hospital centers to ensure better oncological care for pediatric patients<sup>(6)</sup>. All this, following Law 14.238/2021, entitled the Statute of People with Cancer<sup>(7)</sup>.

In this context, this research presents itself as an essential pillar in confronting and promoting more person-centered care by outlining the epidemiological profile of children and adolescents treated at a referral hospital, analyzing anthropometric data, time of diagnosis, family history of cancer, symptomatic manifestations, screening tests, types, treatment, and patient outcomes. Furthermore, we sought to compare results with findings in the literature and to glimpse patterns, trends, as well as gaps in the knowledge studied. Thus, the objective of this study is to analyze the epidemiological profile of children and adolescents diagnosed with leukemia in an oncology center in the capital of Paraíba.

## **METHOD**

It is an observational, retrospective study evaluating medical records at the Napoleão Laureano Hospital in João Pessoa, Paraíba. The institution is a philanthropic institution and a state-recognized cancer treatment center. The research was conducted using a cross-sectional, descriptive, exploratory, and quantitative cohort documentary method using our questionnaire. In addition, anthropometric, clinical, and therapeutic data were collected.

The choice of Hospital Napoleão Laureano is justified by its relevance in the field of oncology, due to the high demand for individuals assisted, as well as the availability of clinical information. The hospital's role as a philanthropic institution highlights its commitment to access to healthcare, especially in critical and complex situations, such as hematologic neoplasms. This dedication reinforces advances in clinical care and the development of public policies aimed at pediatric oncology.

The research collected data from the Medical Archive and Statistics Service (SAME) in the hospital's medical records center, between September and November 2023. With a sample of 83 patients (children and adolescents) admitted during the period from May 2018 to May 2023, a total of 610 medical records of patients with leukemia were selected, in different age groups. It is a non-probabilistic convenience sampling.

The medical records of patients aged between 0 and 17 years with a confirmed diagnosis, belonging to one of the following categories, were included: acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML), according to the International Classification of Diseases (ICD-10): C91.0 (ALL); C91.1 (CLL); C92.0 (AML); C92.1 (CML) (ICD-10, 2023).

The exclusion criteria were based on the removal of medical records that made data collection unfeasible, as well as outcomes outside the defined period.

The following epidemiological data were analyzed: age (minimum 0 years and maximum 17 years 11 months and 29 days), gender (female, male), ethnicity (white, black, brown or Asian), origin (city of origin), weight, height/length and data related to the disease, including family history of cancer. Furthermore, the date of the first consultation, time of onset of symptoms, initial symptomatic manifestations, diagnostic tests, type, treatment, and outcomes were sought.

The data collection was conducted by filling out a form on Google Forms created by the authors, based on information in the medical records, such as admission, progress, prescriptions, reports, complementary exams, and specialist opinions. The collected data were analyzed using descriptive statistics, using Microsoft® Excel and IBM SPSS statistical software, and the results were presented in tables and graphs.

The absolute and/or relative frequencies of the qualitative variables (gender, ethnicity, macro-region) were described. Furthermore, the quantitative variable (age) was represented by mode and median, and the BMI was calculated using the formula (weight/height²). For the bivariate analysis of patient responses, the nominal and continuous independent variables were categorized into groups: "age group" (infant, preschool, school, and adolescent) and "BMI" (low BMI, normal weight, overweight, and obesity)(8).

Thus, the Chi-square test  $(X^2)$  was applied to the patients' questionnaires to assess whether there was an association between each variable – age group, gender, ethnicity, macro-region, weight, height/BMI – and the responses regarding the time between the onset of symptoms and the first consultation, type of cancer, and outcomes. Fisher's exact test was used when appropriate, that is, when cells had a count < 5.

This study applied the Term of Consent authorized by the Teaching and Research Center of Hospital Napoleão Laureano and was registered on the Plataforma Brasil, following the National Research Ethics Committee (CONEP). It should be noted that this research was also submitted to the Ethics Committee of the João Pessoa University Center – UNIPÊ (Opinion: 6,261,817), under the National Health Council (CNS) and Resolution number 466/2012, which, after approval, began data collection. Patients' privacy was respected by keeping the collected information confidential, with it only being accessed by researchers. It is relevant to note that the study did not require an Informed Consent Form (ICF), since it did not identify the individuals involved. Furthermore, all current ethical and legal standards for the use of data in scientific research were followed.

#### RESULTS

After applying the inclusion and exclusion criteria, the study analyzed the medical records of children and adolescents diagnosed with leukemia in the hospital between May 2018 and May 2023. To do this, a sample of 83 cases of patients diagnosed up to 17 years old was selected.

The mean age of the patients was 6.5 years, with the most frequent age being 3 years (mode) and the median being 5 years, as detailed in Table I.

**Table I –** Age range of patients with leukemia at Hospital Napoleão Laureano, from may 2018 to may 2023. João Pessoa, Paraíba, Brazil, 2023.

	Frequency (n)	Percentage (%)	Valid Percentage (%)	Cumulative Percentage (%)
Lactating	10	12.05	12.05	12.05
Preschool	37	44.58	44.58	56.63
School	13	15.66	15.66	72.29
Teenager	23	27.71	27.71	100.0
Total	83	100.0	100.0	

Source: Research Data (2023)

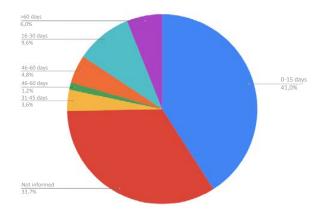
The patients were divided into four groups, according to Table I, that is, infants (under 2 years old) with 12.05%; preschoolers (from 2 to 6 years 11 months and 29 days) with the highest number of cases 44.58%; schoolchildren (from 7 to 9 years 11 months and 29 days) with 15.66%; and adolescents (from 10 to 17 years 11 months and 29 days) with a percentage of 27.71% with the disease. Among those selected, 39 were male (47%) and 44 were female (53%). Regarding ethnicity, 76 (91.6%) were brown, 5 (6%) were white, and 1 (1.2%) black and 1 (1.2%) yellow.

Furthermore, the patients were divided by place of birth. It is worth noting that Paraíba is divided into three health macro-regions: the first encompasses the capital, João Pessoa, and surrounding cities; the second encompasses Campina Grande and the Agreste and Brejo regions; and the third and final macro-region includes the Sertão region (Hinterland), with headquarters in Patos and Sousa<sup>(9)</sup>.

It is noteworthy that macro 1 has the highest number of patients, with 61 (73.5%), followed by macro 3, with 15 (18.1%), and macro 2, with 4 (4.8%). Finally, only 3 patients (3.6%) are of diverse origin, that is, they were born in another Brazilian state.

Among the most frequent group, preschoolers, the minimum weight was 11 kg and the maximum was 27.5 kg, while the median was 17.8 kg. The minimum height in this same group was 87 cm, the maximum was 137 cm, and the median was 110 cm. Regarding Body Mass Index (BMI), considering all groups<sup>(8)</sup>: 50% were eutrophic, 15% of patients were below normal, 35% were above normal, indicating overweight or obesity.

The time between the onset of symptoms and the first appointment showed a modal frequency of 34 patients seen within the first 15 days of symptoms. It is worth noting that the majority of patients started treatment during this period (41%), while others took 16 to 31 days (9.6%), between 31 and 45 days (3.6%), and more than 60 days (6.02%), as shown in Graph 1:



Graph 1: Time count between the onset of symptoms and the first consultation in patients with leukemia at Hospital Napoleão Laureano, from May 2018 to May 2023. João Pessoa, Paraíba, Brazil, 2023. Source: Research data (2023)

Regarding the time from the beginning of symptoms to the first consultation, we had difficulty in the research, since 33.7% did not inform, as shown in Graph 1. In addition, 50.6% of individuals went to their first consultation in less than 30 days.

It was also found that early symptoms in patients with leukemia varied greatly, as shown in Table II.

**Table II** – Early symptoms in leukemia patients at Hospital Napoleão Laureano, from may 2018 to may 2023. João Pessoa, Paraíba, Brazil, 2023.

symptoms	Frequency(n)	Percentage (%)
Fever	55	66.26
BLEEDING, BRUISES, PETECHIAE	29	34.93
paleness	21	25.30
asthenia	20	24.09
Arthralgia	17	20.09
BDOMINAL DISTENSION	12	14.45
loss of weight	8	9.63
LYMPHONOMEDALY	7	8.43
abdominal pain	6	7.22
LOSS OF APPETITE	4	4.81
VOMITING	3	3.61
DIARRHEA OR DYSENTERY	2	2.40
Eyelid edema	2	2.40
CONVULSIVE SEIZURE	2	2.40
HEADACHE	1	1.2
CONSTIPATION	1	1.2
cough	1	1.2
Perioral cyanosis	1	1.2
sleepiness	1	1.2

Source: Research data (2023)

Fever was the most prevalent symptom, reported by 55 patients, as shown in Table II. Bleeding, bruising, and petechiae were the second most frequently reported symptomatic findings. Other manifestations were less frequent.

In the survey of diagnostic exam counts (screening), the most recurrent sets of exams were the following: Complete Blood Count, Myelogram, Immunophenotyping ((30.1%); Complete Blood Count, Myelogram, Immunophenotyping, Molecular Biology (19.3%); Complete Blood Count, Myelogram (7.2%); Complete Blood Count, Myelogram, Immunophenotyping, Molecular Biology, Cytogenetic (4.8%); Complete Blood Count, Myelogram, Immunophenotyping, Cytogenetic (3.6%); Myelogram (3.6%).

Regarding the pathology, acute lymphoblastic leukemia (ALL) was the most common type, present in 62 patients (74.7%). Within this group, the B-ALL subtype was the most prevalent (74.19% or 46 individuals), followed by the T-ALL subtype (11.29% or 7 individuals) and unspecified cases, which represented 14.50% (9 patients). Acute myeloid leukemia (AML) was the second most common type, accounting for 22.9% of cases. The majority of AML cases were unspecified (57.90%). Among the specified cases, subtypes M3 and M4 were the most frequent, representing 21.05% and 10.53% of AML cases, respectively. Subtypes M2 and M5 were less common. These data are illustrated in Table III.

**Table III** – Types and subtypes of leukemia carriers at Hospital Napoleão Laureano, from may 2018 to may 2023. João Pessoa, Paraíba, Brazil, 2023.

	Frequency (n)	Percentage (%)
LLA	62	74.7
SUBTYPE B	46	74.19
SUBTYPE T	7	11.29
UNSPECIFIED	9	14.50
LMA	19	22.9
LMA M2	1	5.26
LMA M3	4	21.05
LMA M4	2	10.53
LMA M5	1	5.26
NOT SPECIFIED	11	57.90
LMC	2	2.4
Total	83	100

Source: Research data (2023)

Chronic myeloid leukemia (CML) was the least common type, accounting for only 2.4% of cases, while acute lymphocytic leukemia (CLL) had no patients, according to Table III. These results provide valuable insight into the prevalence of different types and subtypes of leukemia. However, it is relevant to note that distribution may vary depending on several factors, including the patient population and the hospital's diagnostic practices.

Regarding forms of treatment, the count was as follows: chemotherapy (88% or 73 individuals); chemotherapy, laser therapy (due to GIII mucositis) (1.2%); chemotherapy, bone marrow transplant (7.2% or 6 individuals); chemotherapy, radiotherapy (1.2% or 1 individual); chemotherapy, immunotherapy (1.2% or 1 individual).

Furthermore, regarding the outcome of the patients, 37.3% are in remission (31 individuals); 36.1% are still undergoing treatment (30 individuals). And in a smaller percentage, 26.5% of the patients died (22 individuals), according to Table IV below:

**Table IV** – Outcome of patients with leukemia treated at Hospital Napoleão Laureano, from may 2018 to may 2023. João Pessoa, Paraíba, Brazil, 2023.

-		_
	Frequency (n)	Percentage (%)
N REMISSION	31	37.3
UNDER TREATMENT	30	36.1
DEATH	22	26.5
Total	83	100

Source: Research data (2023)

Among the patients who died, the most prevalent diagnosis was ALL, with a total of 15 patients (68.2%) with ALL to 7 patients who died with AML (31.8%), according to Table IV. Additionally, the individuals who most entered remission had a previous diagnosis of ALL, 22 patients with ALL (71%), 8 with AML (25.8%), and 1 with CML (3.2%).

Regarding information in medical records about family history of cancer, 90.4% of patients were not informed, only 7.2% of patients reported a family history of cancer, and 2.4% had no family history.

Finally, bivariate analysis was performed using the Chi-square test or Fisher's exact test. However, no significant association was found between epidemiological data – age group, gender, ethnicity, macro-region, weight/height, BMI (weight/height²), responses related to time from onset of symptoms to the first consultation, type of leukemia, and outcomes.

## DISCUSSION

The data obtained in this research outlined the compression of the epidemiological profile of a hospital located in Brazil, especially in a less developed northeastern region such as Paraíba. Furthermore, inequalities in access to pediatric oncological health are highlighted, as well as the importance of investments in the public health network, staff qualifications, and the availability of specialized exams.

The average age of patients at Laureano Hospital was 6.5 years, with a higher frequency (mode) of 3 years. Almost 45% of patients belong to the preschool age group (2 to 6 years, 11 months, and 29 days), and among these, the majority present ALL, which corroborates data from the literature, which also identified a higher incidence in this age group<sup>(10,11)</sup>. It is possibly related to genetic factors, as well as the development of the immune system and hematopoietic activity in the first years of life<sup>(12)</sup>.

The sample data showed an almost equal distribution between the genders for the disease, with 47% males and 53% females. It should be noted that, in a similar study, Silva<sup>(13)</sup> demonstrated a higher incidence in the female population, that is, 1.35 times more likely to have ALL. However, this reality differs from several epidemiological studies, in which males are more predominant<sup>(10,11)</sup>.

Estimated data from the João Pessoa Population-Based Cancer Registry for the period 2023 indicated a leukemia rate by gender of 7.67 per 100,000 inhabitants for males and 6.68 per 100,000 for females<sup>(2)</sup>.

Another finding of the research is that more than 90% of children and adolescents diagnosed with leukemia are brown. According to the literature, ethnicity may not have a significant impact on disease prevalence, and more research is needed to explore this relationship<sup>(15)</sup>. Furthermore, in Paraíba, where the majority of the population identifies as brown, the data may only reflect a demographic characteristic, without necessarily indicating a direct relationship with the prevalence of the disease<sup>(26)</sup>. Therefore, the fact that the study was carried out in a philanthropic hospital, the profile, especially the socioeconomic profile of the patients treated, may be aligned with the regional reality of a more economically vulnerable population.

It should be noted that Fonseca<sup>(14)</sup> and Gilio Júnior<sup>(15)</sup>, in research, made an association between ethnicity and leukemia with data reported by the affected pediatric population. Specifically, in the Northeast region, researchers demonstrated that hematologic neoplasia occurs more frequently among brown people. The data in relation to the Northeast region are consistent and reinforce the information found at the Napoleão Laureano hospital, demonstrating a higher incidence<sup>(14,15)</sup> of brown people.

Nationally, the highest number of deaths in Brazil tends to occur among white children and adolescents, with brown children responsible for the second highest rate<sup>(14,15)</sup>. The lowest number is among black, indigenous, and Asian children.

Regarding the geographical distribution of patients, they were classified according to the place of birth, three health macroregions of Paraíba. Most hospital patients belong to macro 1 (73.5%), which includes the capital, João Pessoa, and the surrounding cities. It suggests that the diagnosed population seeks the nearest reference service.

Regarding height and weight, for a better explanation of the data, the Body Mass Index (BMI) was calculated. Of the patients evaluated, 50% were in the normal range, 15% were underweight, and 35% were above normal, indicating overweight or obesity. However, no statistical significance was observed in the association between patients' BMI and the number of deaths in the research carried out at Hospital Napoleão Laureano. Some studies suggest that nutritional status is a determining factor in the mortality of patients admitted to the intensive care unit (ICU), with p < 0.001, in which low-weight patients have a greater chance of death when admitted<sup>(16,17)</sup>.

In 90.4% of medical records, it is not stated whether the patient has a family history of cancer. A possible explanation for this discrepancy is that due attention is not being given or that patients are not being instructed to provide this information. Improvements in the hospital are relevant for training staff in collection and recording, and also educating

patients about the need for this information for their health. This should be noted that the absence of this information may represent a significant gap in medical practice and health promotion. Knowledge can help detect genetic patterns that have not yet been fully understood by science, as well as enable advances, as highlighted by Schmidt et al<sup>(19)</sup>.

Regarding the duration of symptoms, 20% of patients had symptomatic manifestations for a few days, 60% had symptoms for a few weeks or a few months, and 20% had symptoms for several months. As noted by Holanda<sup>(18)</sup>, the clinical manifestations of childhood cancer can vary depending on the type of tumor.

In general, fever, paleness, pain, and weight loss are clinical manifestations of several groups of tumours. Fever is usually the most common symptom in 44.6% of patients diagnosed with leukemia<sup>(18)</sup>. Furthermore, arthralgia, bleeding tendencies, asthenia, and lymphadenomegaly are also important. Therefore, there is a need for technical training of professionals to identify the possibility of cancer quickly, once an adequate history and physical examination reveal the evolution of symptoms and their relationships to diagnose the pathology<sup>(18)</sup>.

Our research corroborates this information, since the most common initial symptoms were: fever (66%), bleeding, bruising, petechiae (35%), bone and joint pain (20%), abdominal distension (15%). These elements are consistent with the known symptoms of leukemia and highlight the importance of early diagnosis for effective treatment<sup>(19)</sup>. Therefore, there is a need for screening protocols in health units for recommendation to reference centers, as well as educational campaigns to raise awareness among parents and guardians about the symptoms of the disease. These actions facilitate rapid interventions and, above all, minimize the impacts of the disease. The combination of these strategies can transform the early disease support scenario in Brazil and contribute to health promotion<sup>(18)</sup>.

Acute leukemias constitute a very heterogeneous group of diseases with different clinical, morphological, immunological, and molecular characteristics, characterized by malignant transformation and uncontrolled proliferation to the level of immature precursor cells (blasts) of the hematopoietic system. As a result, these cells accumulate in the bone marrow and peripheral blood and may migrate and invade other organs. Damage to the myeloid lineage leads to the development of acute myeloid leukemia (AML). Conversely, when the lymphoid lineage is compromised, acute lymphoblastic leukemia (ALL) occurs<sup>(20)</sup>.

Myeloid leukemia is an aggressive tumors that occur in hematopoietic stem cells. The rate of production in the bone marrow, peripheral blood, and other tissues increases, and apoptosis of primitive cells and blast cells decreases, leading to bone marrow failure<sup>(20)</sup>. Its diagnosis depends on the presence of more than 20% of blasts in the blood or bone marrow.

AML is divided into eight subtypes: M0 or undifferentiated acute myeloid; M1 or poorly maturing acute myeloid; M2 or maturing acute myeloid; M3 or promyelocytic acute myeloid; M4 or myelomonocytic; M5 or monocytic acute myeloid; M6 or erythroid; and M7 or megakaryoblastic acute myeloid<sup>(20,21)</sup>. The most common AML in this research at Hospital Napoleão Laureano was AML M3 (21.05%), which agrees with other studies<sup>(22)</sup>.

There are many risk factors for developing AML, the most prominent being: environmental, such as exposure to ionizing radiation, pesticides, benzene, and herbicides; genetic, such as Fanconi anemia, Kosterman syndrome, Wiskott-Aldrich syndrome, Down syndrome, and Klinefelter syndrome<sup>(21)</sup>. Risk factors include the use of medications such as alkylating agents, chloramphenicol, topoisomerase II inhibitors, and methoxypsoralen 10.

Insufficient red blood cell production can cause difficulty breathing when you are weak, tired, or exerting yourself. Severity is related to the degree and speed of onset of anemia. Insufficient white blood cell counts (leukopenia) can lead to infection<sup>(20,21)</sup>. In our study, acute leukemia was the diagnosis (97.6% of cases), with chronic leukemia representing the remaining 2.4%. Thus, the prevalence reported in the most varied literature.<sup>(23,24)</sup>.

According to a study published in the journal Experimental Hematology & Oncology, the incidence of hematologic neoplasia varies according to pathological types and between different populations<sup>(23)</sup>. Globally, while the number of new leukemia cases diagnosed increased from 354,500 in 1990 to 518,500 in 2017, the age-standardized incidence rate (ASIR) decreased by 0.43% per year<sup>(25)</sup>. The number of acute lymphoblastic leukemia (ALL) cases worldwide increased from 49,100 in 1990 to 64,200 in 2017, while ASIR experienced a decrease<sup>(24)</sup>.

Another study published in the same journal showed that the burden of chronic myeloid disease (CML) decreased globally from 1990 to 2017<sup>(24)</sup>. Countries with a higher Social Development Index (SDI) achieved a notable effect in decreasing the burden of CML. However, due to population growth, the incidence and disability-adjusted life years (DALYs) of CML in lower SDI quintiles showed an upward trend<sup>(25)</sup>.

It should be noted that CML presents distinct patterns, depending mainly on age group. This disease is rare in children and adolescents, representing 2% of cases, while CML is more prevalent in the elderly<sup>(26)</sup>. In the study conducted in a pediatric population from an economically disadvantaged state, the inferred incidence was consistent with the global reality, representing 2.4% in the pediatric population.

The State of Paraíba has a Human Development Index (HDI) of 0.698, and is classified as average within the national context; however, it reflects socioeconomic inequalities that impact access to health<sup>(26)</sup>. Furthermore, almost half of the population of Paraíba lives below the poverty line, which dictates the need for public policies aimed at promoting health and reducing inequalities, and providing better care<sup>(26)</sup>.

Studies have shown that the success rate is over 90% when care is initiated early, while delays in initiating care have reduced the success rate to less than 50%<sup>(19)</sup>. However, in the research carried out at Laureano, it was observed that among patients who died, 72% started treatment within the first 15 days after the initial consultation, suggesting that, although early management increases the chances of success, other individual and clinical factors contribute to unfavorable results.

It should be noted that, in many cases, waiting to begin therapy may result in a lower rate of therapeutic success. For example, it was observed that 19.0% of patients who died began therapy management between 16 and 30 days after the first consultation, while 4.8% of deaths had a delay of more than 30 days. Therefore, it is necessary to eliminate long delays, since immediate treatment increases the survival rate.

The adoption of strategies that prioritize diagnosis and rapid initiation of therapy, as well as the elimination of barriers to access, improves clinical outcomes and reduces pediatric mortality rates.

When we analyze the pediatric leukemia mortality rate compared to the data presented, significant disparities are observed that reflect inequalities in access to health care. While mortality in developed countries typically ranges between 5% and 10%, the observed rate of around 26.5% represents a high number<sup>(5)</sup>. These differences can be attributed to factors such as limited access to diagnostics, hospital infrastructure, and socioeconomic inequalities, which are characteristic of the Northeast region of Brazil. In contrast, developed countries have technological advances, greater availability of specialists, and more efficient health policies, which guarantee better outcomes.

According to the scientific literature, for acute leukemias, the average delay in support is aggravating, and it suggests that these diseases often require urgent management and, therefore, have shorter delays compared to other types of childhood cancer<sup>(27)</sup>.

In the specific case of CML, research shows that delaying treatment does not affect the clinical response or survival of patients<sup>(28)</sup>. However, for the same type of disease, immediate care is associated with better survival compared to non-immediate management<sup>(29)</sup>. In childhood ALL, delaying the start of chemotherapy does not lead to an increase in relapse, death, or prolonged hospitalization<sup>(30)</sup>.

For CML cases, patients who were treated earlier had a 60% chance of remission, while those who were treated one year after diagnosis had a 40% chance of remission<sup>(31)</sup>. These data reinforce the need for early diagnosis and demonstrate that with immediate support, there is a greater chance of remission. In the context of a pediatric population in an economically disadvantaged state, difficulties in adequate access may arise. Therefore, public policies, team training, and public awareness that support rapid detection are always welcome, since the time lapse can influence the outcome of the disease. Regarding management, according to scientific literature, depending on the type of leukemia, the molecular alterations found, the patient's age at the time of diagnosis, and the presence of other comorbidities, it is generally carried out through chemotherapy, radiotherapy, immunotherapy, or bone marrow transplant<sup>(32)</sup>.

However, chemotherapy is usually the main supportive option, except for CML, for which active surveillance without chemotherapy is more common in the absence of major complications (anemia or thrombocytopenia)<sup>(32,33)</sup>.

In the study, chemotherapy was the most common treatment (80% of cases), as it is the treatment of choice for ALL, followed by bone marrow transplant (15%) and immunotherapy (5%). Radiation therapy was used in less than 5% of cases<sup>(32,33)</sup>.

When disregarding patients in palliative care, the remission rate in the hospital was approximately 60%. However, according to a survey by the American Cancer Society, the 5-year overall survival rates are around 90% for ALL and 70% for AML (34). ALL, which affects lymphoid cells, generally responds better to available therapies. On the other hand, AML has more complex genetic alterations and resistance, which hinders response and increases relapse rates. Furthermore, ALL is more common in children due to the greater capacity for cellular regeneration and fewer comorbidities. AML is more prevalent in older adults, whose health tends to be weakened, with the presence of immunological decline.

A study published in the journal Scientific Programming highlighted that early detection and diagnosis, i.e., accurate differentiation of malignant leukocytes with minimal costs in the early stages of the disease, is a crucial problem in the field of disease diagnosis<sup>(35)</sup>. The study also mentioned that using machine learning to process leukemia smear images can improve accuracy, reduce diagnosis time, and provide faster, cheaper, and safer diagnostic services<sup>(36)</sup>.

In summary, this research at Laureano Hospital provides valuable data about the demographic profile, diagnosis, treatment, and disease outcomes in patients diagnosed with leukemia. However, despite the efforts of some researchers,

investment remains scarce, limiting the generation of more robust information. Structural precariousness, as well as organizational, technological, and access limitations, impact public health.

Therefore, further studies are needed to confirm these findings and further explore the implications of these results. Considering that the Statute of the Person with Cancer<sup>(7)</sup> (14,238/2021), as well as the law of the National Policy for Pediatric Oncology Care<sup>(8)</sup> (14,308/2022), in its article 8, reinforces research actions in hospital centers, to promote the health of patients, understand the reality and allow improvements. Among the most obvious gaps is the lack of adequate infrastructure in disadvantaged regions, especially in states with low development rates, such as Paraíba, which still lacks financial, technological, and human resources to offer a better quality of service.

## CONCLUSION

The study, carried out at Hospital Napoleão Laureano, provides significant contributions to understanding the epidemiological profile of the child and adolescent population with leukemia in Paraíba, in addition to reinforcing the improvement of diagnostic processes and investments in a poor region. The prevalence of the disease was also observed to be higher in children in the preschool age group (2 to 6 years), with a higher incidence of ALL, data consistent with international literature. Furthermore, the predominance of the brown ethnic group reflects regional demographic characteristics, as well as pointing to possible social inequalities in access to specialized services in the public network.

The research highlighted the urgency of effective strategies to train professionals and raise public awareness about the diagnosis of the pathology. Furthermore, in documented cases, a small proportion of patients began disease support within 15 days of symptoms. In this scenario, the need to eliminate long delays in care is reinforced, as it directly impacts the survival of the person being assisted.

The mortality observed in the study was high, compared to the global average for developed countries. It demonstrates the need for continuous improvements in disease management. Furthermore, the scenario reflects regional inequalities in access to cancer healthcare and highlights the need for urgent interventions to ensure comprehensive and timely care for children and adolescents. Therefore, limitations, especially those related to human resources, inequalities, and infrastructure, must be considered when developing public policies aimed at health.

Therefore, the information obtained indicates intersectoral approaches in tackling pediatric leukemia, through professional training, social assistance, and education that enhance early detection and adherence to clinical management. The importance of forming support networks with family members and community involvement is also highlighted in order to promote quality of life and minimize psychosocial impacts. Furthermore, it is essential to invest in the continuity of research in this field, focusing on regional peculiarities and inequalities, aiming to generate new knowledge.

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The authors have reported no conflict of interest.

## CONTRIBUTIONS

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