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Clinical characteristics and complications in children and adolescents with hyperleukocytic acute leukemia

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ABSTRACT

Introduction. Hyperleukocytic acute leukemia is a pediatric hematological-oncological emergency associated with high morbidity and mortality.

Objective. To describe the clinical and hematological characteristics, complications, and treatments of patients with acute hyperleukocytic lymphoblastic or myeloid leukemia.

Population and methods. Descriptive, retrospective, cross-sectional study conducted in a tertiary pediatric hospital between January 1, 2020, and December 31, 2024.

Results. Twenty-one patients <15 years of age diagnosed with hyperleukocytic leukemia were analyzed. Fifty-six percent had type B acute lymphoblastic leukemia, and 62% had extramedullary manifestations such as hepatomegaly and splenomegaly. The most common complications were tumor lysis syndrome (71%) and leukostasis (28%); 76% received rasburicase, and 1/3 required leukapheresis; 90% began chemotherapy within the first 2 days of hospitalization. There was a single early death due to hemorrhage in the central nervous system.

Conclusion. The importance of early diagnosis and intensive initial management to improve the clinical outcomes of these high-risk patients is highlighted.

Keywords: *leukocytosis; leukostasis; acute lymphocytic leukemia; tumor lysis syndrome.*

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INTRODUCTION

Acute leukemias are the most common oncological diseases in pediatrics. They account for 37% of all malignant diseases in children under 15 years of age.[1]

Hyperleukocytosis, defined as a white blood cell count greater than 100 000/mm³, is an unfavorable prognostic factor in acute leukemias and is associated with poorer clinical outcomes and increased early mortality.[2,3]

The most common complications of hyperleukocytic leukemia (HL) are acute tumor lysis syndrome (ATLS), leukostasis, and disseminated intravascular coagulation. Given the high risk of ATLS, therapeutic measures should be initiated promptly to prevent it. Elevated lactate dehydrogenase (LDH) levels are an indirect marker of high tumor burden and a useful predictor of ATLS risk. Specific agents such as allopurinol or rasburicase are required to control hyperuricemia. When conservative treatment fails to normalize electrolyte disturbances or restore urinary flow, dialysis is indicated.[4-7]

Hyperleukocytosis can cause leukostasis, leading to tissue hypoxia, vascular damage (thrombosis), organ dysfunction, and/or hemorrhage, primarily affecting the lungs, kidneys, and central nervous system (CNS). Leukostasis is an emergency and requires rapid recognition and initiation of treatment to prevent renal or respiratory failure and intracranial hemorrhage. Treatment includes conservative interventions such as hyperhydration with twice the baseline volume and potassium-free solutions associated with early initiation of chemotherapy. The latter is a safe way to reduce white blood cells; when definitive treatment of the disease is not possible, cytoreduction with chemotherapy, including corticosteroids, hydroxyurea, or low-dose cytarabine, can be initiated. Less than 5% of children require mechanical cytoreduction such as leukapheresis or exchange transfusion, which are rapid and effective strategies for reducing white blood cells; however, their use is controversial.[8-15] The objective of this study is to describe the clinical and hematological characteristics, complications, and treatments of patients admitted to the Hospital Interzonal de Agudos Especializado en Pediatría Sor María Ludovica with acute lymphoblastic or myeloid leukemia.

POPULATION AND METHODS

Data were included from patients with a first event of HL (lymphoblastic or myeloid) (white blood cells >100 000/mm³) diagnosed at the Hospital Interzonal de Agudos Especializado en Pediatría Sor María Ludovica, La Plata (Argentina) between January 1, 2020, and December 31, 2024.

The variables analyzed were as follows:

- Baseline clinical characteristics: age, sex, cancer diagnosis, and extramedullary involvement. Hematological characteristics: thrombocytopenia, anemia, and coagulation disorders.
- Complications: ATLS, CNS bleeding or thrombosis, and leukostasis.
- Treatments received: use of rasburicase, dialysis therapy, chemotherapy, and leukapheresis.

The number of days between patient admission and the start of chemotherapy was recorded.

Data collection was performed by reviewing medical records; the data obtained were entered into a database designed for this study.

Quantitative variables are described using measures of central tendency (mean and standard deviation, or median and interquartile range), depending on whether they are normally distributed. For qualitative variables, frequencies and percentages are reported.

The Institutional Review Board approved the protocol for Research Protocols on February 20, 2025.

RESULTS

The medical records of 21 patients were analyzed. *Table 1* shows the clinical and hematological characteristics of the patients included in the study.

Only 2 of 21 patients had a white blood cell count greater than 400 000/mm³ at baseline; 9 had counts between 100 000/mm³ and 199 999/mm³; and 10 had between 200 000/mm³ and 399 999/mm³. 13 of 21 children had anemia associated with hyperleukocytosis, and all of them had thrombocytopenia. The initial LDH value ranged from 591 IU/L to 40 377 IU/L, with a mean of 5150 for a normal LDH value between 338-820 IU/L.

Table 2 shows the complications and treatments received by the patients.

Only one case of early mortality within the first 14 days was reported, which was secondary to CNS hemorrhage; it was a girl with thrombocytopenia and coagulation disorder from the moment of admission.

Table 1. Clinical and hematological characteristics of patients

Variable	n = 21
Age (years)	
<1	2
1-10	13
>10	6
Gender	
Male	15
Female	6
Diagnosis	
Myeloid leukemia	3
Lymphoblastic leukemia	18
B-cell lymphoblastic leukemia	10
T-cell lymphoblastic leukemia	8
Extramedullary involvement	
Splenomegaly	13
Hepatomegaly	13
Adenomegaly	9
Enlarged mediastinum	5
Abdominal mass	1
Nephromegaly	1
CNS involvement	4
Hematological characteristics	
Thrombocytopenia	21
Anemia	13
Impaired coagulation	11

CNS: central nervous system.

Six of the 21 children had symptoms consistent with leukostasis, five had respiratory symptoms, and one had CNS involvement.

In our series, one-third of patients underwent leukapheresis, and 16 of 21 received rasburicase due to high risk of ATLS and hyperuricemia.

All children with lymphoblastic leukemia began cytoreduction with corticosteroids; only

Table 2. Results

Variable	n = 21
Complications	
Early mortality	1
Tumor lysis syndrome	15
CNS thrombosis	0
CNS bleeding	3
Leukostasis	6
Treatments	
Leukapheresis	7
Dialysis therapy	0
Use of rabicurase	16
Cytoreduction with chemotherapy	21
Corticosteroids	18
Cytarabine	3
Hydroxyurea	5

CNS: central nervous system.

2/21 required hydroxyurea in combination to reduce white blood cell counts due to initial lack of response to corticosteroids. All patients with myeloid leukemia underwent cytoreduction with low-dose cytarabine, with 2 patients receiving it in combination with hydroxyurea.

Regarding the start time of cytoreductive treatment, it ranged from 1 to 5 days (median of 36 hours) from admission; 19/21 started within the first 2 days.

DISCUSSION

In our population, the most common cancer was B-ALL, as in other studies.[8,15]

Among the extramedullary manifestations, the most frequent in our patients were hepatomegaly and splenomegaly, which coincides with Kittivisut.[5] In half of the patients, we found a combination of hepatomegaly and splenomegaly, and in 4/21, CNS involvement was found.

The hematological characteristics were similar to those observed in other pediatric leukemias. Unlike others, more than half (11/21) of the patients had laboratory coagulation abnormalities; the most frequent abnormality was decreased prothrombin concentration, without correlation with clinical findings, so they did not require treatment.[3]

Among the most frequent complications related to hyperleukocytosis, disseminated intravascular coagulation, thrombosis, ATLS, and leukostasis have been described,[2,8,9,15], coinciding with ATLS as the most frequent complication in the studied population; in all cases, hyperuricemia was the main finding. The average LDH value at baseline was higher than that reported by other authors.[8,9]

We had a higher use of rasburicase (16/21) than in other studies.[8,9,15] It should be noted that the use of rasburicase depends largely on each institution and on the accessibility of treatments.

In our study, 7/21 patients underwent leukapheresis. This percentage is higher than its use in other populations. [8,11,15]

Although in this study 90% of patients started chemotherapy within the first 2 days of hospital admission, the median time to initiation was 1.5 days, almost twice that observed in Lowe's study,[9] in which the median time to initiation was 1 day.

During the period evaluated, there was one death within the first 14 days of admission, which was secondary to CNS bleeding, as in Wald's study,[4] in which mortality was secondary to hemorrhage. In Wald study, three of four patients had CNS bleeding, and one had pulmonary hemorrhage. Unlike what we report, the patients in his series with bleeding did not have severe thrombocytopenia or coagulation disorders, as in our study. Abla[8] reports 3.5% of CNS bleeding, more frequent the higher the white blood cell count at baseline, similar to what Lowe[9] describes, which is a 2% incidence of CNS hemorrhage more frequent in AML, and all patients with bleeding had extreme hyperleukocytosis.

CONCLUSION

This study enabled the detailed characterization of pediatric patients with HL treated at a referral hospital. Frequent complications included ATLS and leukostasis, the latter being particularly relevant due to its potential severity. The high proportion of patients who received rasburicase and the indication for leukapheresis in one-third of cases reflect the complexity of initial therapeutic management and the need for an intensive approach to prevent major complications.

Having the resources to support cancer patients helps prevent and alleviate complications, contributing to a more favorable outcome.

The relevance of these results lies in the up-to-date local information they provide on a specific high-risk pediatric population, which is essential for adjusting therapeutic strategies, optimizing resource use, and timing treatment initiation. ■

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