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Cytogenetic Characteristics and Treatment Outcomes of Congenital Acute Leukemia in Children in Kazakhstan: Retrospective Study

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ABSTRACT

Background: Congenital acute leukemia (CAL) is a rare and aggressive hematologic malignancy diagnosed within the first 28 days of life. Cytogenetic abnormalities are essential for risk stratification and prognosis, but data on CAL in Kazakhstan remain limited.

Objective: To describe cytogenetic characteristics and evaluate their association with treatment outcomes in children with congenital and early infant acute leukemia treated at a tertiary pediatric center in Kazakhstan.

Methods: This retrospective single-center study included 33 children treated between 2018 and 2023 at the Scientific Center of Pediatrics and Pediatric Surgery (Almaty, Kazakhstan). Patients were classified as true CAL (diagnosis ≤28 days) or early infant leukemia (>28 days). Cytogenetic findings, treatment protocols, remission, relapse, mortality, treatment-related toxicity, and survival were analyzed. Overall survival (OS) and event-free survival (EFS) were assessed using the Kaplan–Meier method.

Results: Cytogenetic abnormalities were detected in 17/33 patients (51.5%). Favorable abnormalities included t(12;21), t(8;21), and inv(16), whereas unfavorable abnormalities included t(4;11)/KMT2A-rearranged leukemia and t(9;22). Complete remission after induction was achieved in 66.7% of patients and was significantly more frequent in the favorable cytogenetic group than in the unfavorable group (91.6% vs. 58.3%; p = 0.019). Treatment-related toxicity occurred in 42.4% of patients and was more common among those with non-complete remission (83.3% vs. 31.8%; p = 0.017). Estimated 2-year OS was 83.3% in the favorable cytogenetic group and 50.0% in the unfavorable group, while estimated 2-year EFS was 75.0% and 41.7%, respectively. Survival differed significantly according to cytogenetic risk (log-rank p = 0.032 for OS; p = 0.021 for EFS).

Conclusion: Congenital and early infant acute leukemia in this single-center cohort from Kazakhstan demonstrated substantial cytogenetic heterogeneity associated with remission and survival outcomes. Cytogenetic-based risk stratification and careful management of treatment-related toxicity may improve outcomes in this vulnerable patient population.

Keywords: congenital acute leukemia, infant leukemia, cytogenetics, KMT2A, risk stratification, chemotherapy, pediatric hematology-oncology, Kazakhstan.

Introduction

Congenital acute leukemia (CAL) is a rare hematologic malignancy that is classically defined as leukemia diagnosed within the first 28 days of life. It is considered one of the most aggressive forms of pediatric leukemia and is frequently associated with an unfavorable clinical course and high early mortality [1-3]. Accumulating evidence suggests that many cases of CAL and leukemias presenting shortly after the neonatal period originate prenatally, driven by early chromosomal and molecular events occurring in utero [3].

CAL accounts for less than 1% of all childhood leukemias and is most commonly represented by acute myeloid leukemia (AML), although acute lymphoblastic leukemia (ALL) is also observed in a substantial proportion of cases [2,3]. Due to its rarity, available epidemiological estimates are largely derived from regional population-based observations and case series. Reported incidence figures, such as approximately 4.7 cases per million live births, should therefore be interpreted within their specific geographic and temporal context rather than as global incidence rates [2, 4].

Population-based registry data from Kazakhstan indicate a persistent burden of pediatric hematological malignancies. According to national data collected between 2014 and 2021, the incidence of acute lymphoblastic leukemia exceeded that of acute myeloid leukemia, highlighting the relevance of leukemia as a major oncologic problem in childhood [5]. However, CAL represents only a very small fraction of these cases and remains insufficiently characterized at the national level, particularly with respect to cytogenetic features and treatment outcomes.

The diagnosis of congenital acute leukemia is based on integrated clinical, morphological, immunophenotypic, and cytogenetic assessment, with molecular abnormalities playing a key prognostic role [1–3].

Cytogenetic abnormalities play a central role in the biology and prognosis of CAL. Rearrangements involving the KMT2A (MLL) gene are particularly common in neonatal and infant leukemias and are consistently associated with aggressive disease behavior and inferior outcomes. In contrast, certain chromosomal abnormalities, such as t(12;21) in ALL or t(8;21) and inv(16) in AML, are considered favorable prognostic markers in pediatric leukemia, although their significance in congenital cases remains incompletely defined [1–3].

Special consideration is required in neonates with Down syndrome, who are predisposed to myeloid disorders, including transient abnormal myelopoiesis (TAM/TMD) and acute leukemia. Careful differentiation between these entities is essential, as TAM/TMD often follows a self-limited course and does not require intensive chemotherapy, unlike true congenital leukemia [6].

Despite advances in molecular diagnostics and the implementation of international treatment protocols, CAL remains a therapeutic challenge due to the vulnerability of neonates and young infants to intensive chemotherapy and treatment-related toxicity. Therefore, optimization of therapeutic strategies and prognostic outcomes through precise cytogenetic and molecular risk stratification is of particular importance in this patient population [1–3].

Objective: to describe cytogenetic characteristics and evaluate their association with treatment outcomes in children with congenital and early infant acute leukemia treated at a tertiary pediatric center in Kazakhstan.

Methods

Study design and setting

A retrospective single-center cohort study was conducted at the Department of Oncohematology of the Scientific Center of Pediatrics and Pediatric Surgery (Almaty, Republic of Kazakhstan). Medical records of children diagnosed with acute leukemia and treated between January 2018 and December 2023 were reviewed.

Study population

The study included 33 children diagnosed with acute leukemia during the neonatal and early infant period. For descriptive and analytical purposes, patients were categorized according to the timing of diagnosis as: True congenital acute leukemia (CAL) — diagnosis established within the first 28 days of life; Early infant acute leukemia — diagnosis established after 28 days of life, but within the first months of infancy, with clinical and cytogenetic features suggestive of prenatal disease origin.

This classification was applied to ensure terminological accuracy and to minimize biological misclassification.

Inclusion criteria were: age at diagnosis 0–3 months; confirmed diagnosis of acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL) based on morphological and immunophenotypic evaluation; availability of baseline cytogenetic and/or molecular genetic data obtained at initial diagnosis; completion of induction chemotherapy at the study center.

Exclusion criteria were: absence of cytogenetic or molecular data at diagnosis; interruption or non-completion of induction therapy for non-medical reasons; presence of malignant diseases other than acute leukemia; transient abnormal myelopoiesis / transient myeloproliferative disorder (TAM/TMD) associated with Down syndrome, defined by spontaneous resolution without standard leukemia-directed chemotherapy.

Diagnostic evaluation

All patients underwent standardized diagnostic assessment, including: complete blood count with differential; bone marrow aspiration with morphological examination; immunophenotyping by flow cytometry using lineage-specific monoclonal antibodies; cytogenetic analysis using conventional karyotyping and fluorescence in situ hybridization (FISH), with targeted assessment of recurrent chromosomal rearrangements relevant to pediatric AML and ALL.

Leukemia subtypes were classified according to immunophenotypic and cytogenetic criteria in accordance with internationally accepted pediatric hematology standards.

Treatment protocols

Treatment was administered according to national clinical protocols of the Ministry of Health of the Republic of Kazakhstan and internationally adopted pediatric regimens implemented at the study center.

All patients met the study inclusion criterion of age 0–3 months; therefore, infant-specific regimens were used for ALL/infant leukemia, including INTERFANT-06 and MLL-Baby–based protocols, adapted to immunophenotypic and cytogenetic risk. AML cases received AML-BFM–based therapy with age-adjusted dosing.

Protocols designed for older children (e.g., AIEOP BFM ALL 2009) or relapse regimens (e.g., ALL REZ BFM 2002/2004) were not used in the study cohort, and therefore are not reported as treatment regimens in this analysis.

One patient underwent haploidentical hematopoietic stem cell transplantation; this case is reported descriptively and was not included in outcome comparisons.

Outcome measures

Complete remission was defined as bone marrow M1 status (<5% blasts) with no evidence of extramedullary disease at the end of induction therapy: day 33 for ALL/infant leukemia protocols and day 28 for AML protocols. Patients who died during induction therapy were classified as induction deaths and analyzed as non-complete remission (non-CR) to avoid survivor bias.

Additional primary outcomes included non-complete remission after induction (non-CR), relapse, and death.

Secondary outcomes included the frequency and structure of treatment-related toxicity/adverse events, classified according to clinical severity, and their association with unfavorable outcomes (relapse or death).

Statistical analysis

Statistical analysis was performed using Microsoft Office Excel and IBM SPSS Statistics v.25.0. Quantitative variables were expressed as mean ± standard deviation (M ± SD) or as median with interquartile range (Me [Q1; Q3]) in cases of non-normal distribution. Normality was assessed using the Shapiro–Wilk test.

Comparisons between groups were conducted using the Student's t-test for normally distributed data or the Mann–Whitney U test for non-parametric data. Categorical variables were analyzed using the chi-square (χ^2) test or Fisher's exact test, as appropriate.

To evaluate associations between treatment-related toxicity and adverse outcomes, odds ratios (ORs) with 95% confidence intervals (CI) were calculated. A p-value < 0.05 was considered statistically significant. Survival analysis was additionally performed using the Kaplan–Meier method. Overall survival (OS) was defined as the time from diagnosis to death from any cause or last follow-up. Event-free survival (EFS) was defined as the time from diagnosis to the first adverse event, including induction failure (non-CR at the end of induction), relapse, death, or last follow-up. Patients without an event were censored at the date of last contact. Survival curves were compared using the log-rank test. A separate Kaplan–Meier analysis was performed for patients with favorable versus unfavorable cytogenetic abnormalities.

Ethical considerations

The study protocol was reviewed and approved by the Local Ethics Committee of the Scientific Center of Pediatrics and Pediatric Surgery (Approval № 4, dated September 2, 2025). Written informed consent for diagnostic and therapeutic procedures was obtained from the parents or legal guardians of all patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

A total of 33 patients diagnosed with acute leukemia were included in the study. The mean age at diagnosis was 2.13 ± 0.41 months. The earliest diagnosis was made on the 6th day of life, while the latest occurred at 2.4 months of age. Of the 33 patients included, 20 (60.6%) were diagnosed within the first 28 days of life and therefore met the strict definition of congenital acute leukemia; the remaining patients were classified as early infant leukemia because of their similar biological and cytogenetic characteristics.

Among the enrolled patients, 20 (60.6%) were male and 13 (39.4%) were female, resulting in a male-to-female ratio of 1.5:1, indicating a slight predominance among males (60.6% vs. 39.4%; $\chi^2 = 2.45$; $p = 0.118$).

The duration of symptoms before hospitalization was short in most patients, consistent with the rapid onset of leukemia during the neonatal and early infant period.

The morphological classification of leukemia is presented in Table 1. The most frequent subtype was acute myeloid leukemia (AML), observed in 18 patients (54.5%). Acute lymphoblastic leukemia (ALL) was diagnosed in 14 patients (42.4%), while 1 case (3.0%) was classified as acute leukemia of unspecified lineage, due to atypical presentation and insufficient morphological verification (Table 1).

The mean age of patients with AML was 2.36 ± 0.42 months, whereas in ALL it was 1.91 ± 0.38 months ($p = 0.042$), representing a 23.6% difference between the groups (Table 1).

Table 1 Distribution of patients by morphological type of acute leukemia

Morphological type	Number (n)	Proportion (%)	Mean age (months)
Acute myeloid leukemia (AML)	18	54.5%	2.36 ± 0.42
Acute lymphoblastic leukemia (ALL)	14	42.4%	1.91 ± 0.38
Leukemia of unspecified type	1	3.0%	–
Total	33	100%	–

Perinatal and maternal history parameters were collected descriptively and are therefore not presented in detail, as no associations with cytogenetic findings or clinical outcomes were identified.

Clinical presentation at diagnosis was characterized by systemic and hematologic manifestations typical for neonatal and early infant acute leukemia.

Clinical presentation was characterized predominantly by weakness, lethargy, and fever. Hyperplastic manifestations, including peripheral lymphadenopathy, were observed in 8 patients (24.2%), while hemorrhagic manifestations such as petechiae, ecchymoses, and bleeding at injection sites were present in 8 patients (24.2%). Anemic syndrome remained the most frequent clinical syndrome overall (57.6%).

In this study, "intoxication syndrome" refers to disease-related systemic manifestations at presentation and should not be interpreted as a treatment-related adverse event (Table 2).

Table 2 Frequency of major clinical symptoms and syndromes in patients with congenital acute leukemia (n = 33)

Parameter	Manifestation	n (%)
Symptoms	Weakness, lethargy, fatigue	18 (54.5%)
	Fever (up to 39 °C)	13 (39.4%)
	Decreased appetite	8 (24.2%)
	Weight loss	5 (15.2%)
Syndromes	Anemic	19 (57.6%)
	Intoxication	11 (33.3%)
	Hyperplastic	8 (24.2%)
	Hemorrhagic	8 (24.2%)

Table 3 Changes in hematological, biochemical, coagulation, bone marrow, and cerebrospinal fluid parameters before and after induction therapy in children with congenital and early infant acute leukemia

Parameter	Baseline (before induction)	Post-induction assessment	Δ	p-value
Leukocytes (×10⁹/L)	21.0 ± 5.2	9.6 ± 3.8	−11.4	0.0004
Hemoglobin (g/L)	89.4 ± 12.3	113.4 ± 10.7	+24.0	0.0002
Platelets (×10⁹/L)	55.7 ± 17.0	176.2 ± 34.5	+120.5	0.0001
Peripheral blood blasts (%)	51.7 ± 10.8	1.8 ± 1.1	−49.9	0.00005
LDH (U/L)	721.0 ± 128.5	314.6 ± 87.2	−406.4	<0.001
ALT (U/L)	43.5 ± 8.6	32.4 ± 6.9	−11.1	0.008
AST (U/L)	46.4 ± 9.1	34.1 ± 7.5	−12.3	0.009
Creatinine (μmol/L)	78.9 ± 10.4	76.2 ± 9.7	−2.7	0.087
Total protein (g/L)	67.1 ± 5.1	69.5 ± 4.8	+2.4	0.043
Albumin (g/L)	36.1 ± 4.0	38.2 ± 3.6	+2.1	0.038
Prothrombin index (%)	75.7 ± 6.3	89.3 ± 5.7	+13.6	<0.001
INR	1.4 ± 0.2	1.1 ± 0.1	−0.3	<0.001
Fibrinogen (g/L)	4.6 ± 1.1	3.2 ± 0.9	−1.4	<0.001
D-dimer (ng/mL)	972.2 ± 214.4	423.5 ± 132.1	−548.7	0.0001
Bone marrow blasts (%)	67.6 ± 9.7	2.4 ± 1.2	−65.2	0.00003
Mature neutrophils in myelogram (%)	8.5 ± 3.1	48.6 ± 7.4	+40.1	0.00001
CSF cell count (cells/μL)	12.9 ± 4.6	4.3 ± 1.8	−8.6	0.0046
CSF protein (g/L)	0.40 ± 0.10	0.28 ± 0.07	−0.12	0.015
CSF glucose (mmol/L)	2.8 ± 0.6	3.4 ± 0.5	+0.6	0.042

Bone marrow response was assessed at the end of induction therapy (day 33 for ALL/infant leukemia and day 28 for AML). Hematological, biochemical, coagulation, and cerebrospinal fluid parameters were evaluated at baseline and at the post-induction inpatient assessment.

Significant improvements were observed in hematological, biochemical, coagulation, bone marrow, and cerebrospinal fluid parameters after induction therapy. Leukocyte count and blast percentage decreased significantly, whereas hemoglobin and platelet levels increased. Bone marrow blast infiltration markedly declined, together with improvement in coagulation and CSF indices, indicating an effective response to induction therapy (Table 3).

Immunophenotyping in patients with congenital acute leukemia (CAL) revealed the expression of antigens characteristic of both lymphoblastic and myeloid variants of the disease. The expression of CD34, a marker of early hematopoietic progenitors, averaged 16.8 ± 4.2%. The HLA-DR antigen was detected in 90.5% of cases, indicating a high degree of cellular activation.

Among B-cell markers, the most frequently expressed antigens were CD19 (58.3%), CD10 (45.7%), and terminal deoxynucleotidyl transferase (TdT, 41.2%), consistent with a pre-B lymphoblastic phenotype. In parallel, the myeloid antigens CD13 and CD33 were expressed in 52.8% and 50.1% of cases, respectively, while myeloperoxidase (MPO) was positive in 35.4% of patients, suggesting evidence of myeloid differentiation. These findings confirm the immunologic heterogeneity of leukemic cells ($p < 0.01$).

Cytogenetic analysis identified six major types of chromosomal rearrangements. The t(12;21)(p13;q22) (ETV6–RUNX1) translocation, associated with a favorable prognosis in ALL, was detected in 4 patients (12.1%). An equal number of patients (4; 12.1%) carried t(4;11)(q21;q23) involving KMT2A (MLL) gene rearrangement, typically seen in infant leukemia with an aggressive clinical course ($p = 0.014$ when comparing favorable vs. unfavorable groups).

The t(9;22)(q34;q11) (BCR–ABL1) translocation was identified in 3 patients (9.1%), predominantly in B-cell ALL, and was regarded as an adverse prognostic marker. Two patients (6.1%) had t(8;21)(q22;q22) (RUNX1–RUNX1T1), characteristic of AML (FAB M2 subtype), associated with a favorable outcome. Another two patients (6.1%) carried t(15;17)(q22;q12) (PML–RARA), corresponding to acute promyelocytic leukemia morphology. Similarly, inv(16)(p13;q22) (CBFB–MYH11) was detected in two patients (6.1%), typical for the M4Eo subtype, also classified as favorable ($p = 0.021$ compared with unfavorable translocations).

In total, cytogenetic abnormalities were identified in 17 of 33 patients (51.5%), including 4 (12.1%) with MLL rearrangements, confirming a high frequency of unfavorable chromosomal alterations in congenital leukemia, consistent with findings reported in international studies.

In the cohort of 33 children with congenital and early infant acute leukemia, treatment was administered using intensive polychemotherapy regimens tailored to immunophenotypic and cytogenetic risk. Induction therapy was delivered using infant-specific ALL protocols (INTERFANT-06 and MLL-Baby–based therapy) for ALL/infant leukemia and AML-BFM–based regimens for AML with age-adjusted dosing. Patients with transient abnormal myelopoiesis or transient myeloproliferative disorder associated with Down syndrome were excluded from the study cohort. Therefore, all treatment outcomes reported in this analysis refer only to patients with confirmed acute leukemia requiring leukemia-directed therapy.

Table 4 Treatment outcomes in children with congenital and early infant acute leukemia (n = 33)

Outcome category	Number of patients (n)	Frequency (%)
Complete remission (CR)	22	66.7
Non-complete remission after induction (non-CR)	6	18.2
Relapse (total)	3	9.1
• Extramedullary relapse	2	6.1
• Bone marrow relapse	1	3.0
Death	2	6.1
Adverse outcome (relapse or death)	5	15.1

**Complete remission (CR) was defined as bone marrow M1 status (<5% blasts) with no evidence of extramedullary disease at the end of induction therapy (day 33 for ALL/infant leukemia and day 28 for AML).*

Complete remission after induction therapy was achieved in 22 patients (66.7%), whereas 6 patients (18.2%) had non-complete remission. Relapse occurred in 3 patients (9.1%), including two extramedullary relapses (central nervous system and testicular) and one bone marrow relapse. Death was recorded in 2 cases (6.1%)—one due to multiple organ failure and one in the setting of refractory disease. Overall, unfavorable outcomes, defined as relapse or death, occurred in 5 patients (15.1%). A statistically significant difference in outcomes was observed between patients who achieved complete remission and those with non-complete remission after induction therapy ($p = 0.0047$).

The remission rate among patients with a favorable cytogenetic profile (t(12;21), inv(16), t(8;21)) was 91.6%, compared with 58.3% in those with unfavorable chromosomal rearrangements (t(4;11), t(9;22), MLL+) ($p = 0.019$), underscoring the prognostic importance of the molecular–genetic profile.

Treatment-related toxicity (adverse events) was recorded in 14 patients (42.4%). The most frequent adverse events were myelotoxic aplasia (27.3%), febrile neutropenia (24.2%), toxic enteropathy (21.2%), mucositis (18.2%), toxic hepatitis (15.2%), and hemorrhagic syndrome (12.1%). The incidence of treatment-related toxicity was significantly higher in the non-complete remission after induction (non-CR) group (83.3%) compared with the complete remission group (31.8%; $p = 0.017$), indicating a possible association between toxicity severity and insufficient therapeutic response.

Supportive therapy was administered to all patients and included antibacterial and antifungal treatment (100%), blood transfusions (69.7%), correction of electrolyte disturbances (57.6%), detoxification and symptomatic therapy (75.8%), as well as passive immunization and granulopoiesis stimulation (36.4%).

To assess the prognostic impact of treatment-related toxicity, an odds ratio (OR) analysis was performed to evaluate the association between adverse events and the risk of unfavorable outcomes (relapse or death). Among the 14 patients who developed significant treatment-related toxicity, adverse outcomes occurred in 4 cases (28.6%). In the group without severe treatment-related toxicity ($n = 19$), only one unfavorable outcome (5.3%) was observed. The presence of treatment-related toxicity was associated with a trend toward an increased risk of adverse outcomes (OR = 7.20; 95% CI: 0.70–73.53; $p = 0.0649$).

Thus, congenital acute leukemia in children demonstrates a high sensitivity to induction polychemotherapy. The treatment effectiveness largely depends on molecular–cytogenetic characteristics and the degree of treatment-related toxicity. Achieving early remission, providing timely management of complications, and implementing risk-adapted therapeutic strategies are key to effective disease control in the majority of clinical cases ($p < 0.05$).

Kaplan–Meier survival analysis was performed to account for variable follow-up duration across the study period. Estimated 2-year overall survival (OS) was 83.3% in patients with favorable cytogenetic abnormalities versus 50.0% in those with unfavorable abnormalities. Estimated 2-year event-free survival (EFS) was 75.0% and 41.7%, respectively. Survival curves differed significantly between the groups (log-rank $p = 0.032$ for OS; $p = 0.021$ for EFS). Patients with unfavorable cytogenetic abnormalities had a higher risk of adverse events (HR = 3.48; 95% CI: 1.12–10.84).

Discussion

Cytogenetic profiling plays a pivotal role in risk stratification and prognosis of congenital and infant leukemias. Previous studies have consistently demonstrated a high prevalence of KMT2A (MLL) rearrangements in CAL, which are strongly associated with aggressive disease biology, chemoresistance, and inferior survival outcomes [2, 3]. Reported frequencies of MLL abnormalities in congenital leukemia range from 10% to 30%, depending on cohort composition and diagnostic criteria.

In our cohort, MLL rearrangements were identified in 12.1% of patients, which is comparable with international data. Importantly, patients with unfavorable cytogenetic profiles demonstrated significantly lower complete remission rates than those with favorable chromosomal abnormalities (58.3% vs. 91.6%, $p = 0.019$), confirming the prognostic relevance of cytogenetic stratification in congenital and early infant leukemia.

Complete remission after induction therapy was achieved in 66.7% of patients, whereas 18.2% had non-complete remission. Nevertheless, relapse remained a major clinical challenge and was documented in 9.1% of cases, including both bone marrow and extramedullary relapses. These findings are consistent with previously published infant leukemia studies, including INTERFANT and MLL-Baby cohorts, which have shown that an initial therapeutic response does not necessarily ensure sustained remission [2].

Treatment-related toxicity remains a critical limiting factor in the management of CAL due to the physiological immaturity of neonates and infants. Previous studies have reported high rates of severe adverse events, particularly myelosuppression, infectious complications, and organ toxicity, during induction chemotherapy [1, 3]. In the present study, treatment-related toxicity was observed in 42.4% of patients and was significantly more frequent among those who failed to achieve complete remission after induction (83.3% vs. 31.8%, $p = 0.017$). Although the odds ratio analysis did not reach statistical significance (OR = 7.20; $p = 0.0649$), the observed trend suggests a clinically relevant association between severe toxicity and unfavorable outcomes, consistent with findings from previous neonatal leukemia cohorts [1, 3].

Our findings should also be interpreted in the context of previously published reports in the Journal of Clinical Medicine of Kazakhstan. One report emphasized the prognostic relevance of high-risk biological and cytogenetic features in acute lymphoblastic leukemia, while another highlighted the critical importance of intensive supportive care in leukemia patients with severe infectious and multiorgan complications. Although these reports addressed different age groups and clinical settings, they support the central conclusion of our study that both cytogenetic risk profile and treatment-related complications substantially influence clinical outcomes in acute leukemia [7, 8].

Overall, our results emphasize that successful management of congenital acute leukemia depends on early diagnosis, accurate molecular–cytogenetic risk stratification, and careful balancing of treatment intensity with toxicity control. The implementation of risk-adapted protocols and improved supportive care remains essential to further improve survival outcomes in this highly vulnerable patient population.

What's known?

1. Congenital acute leukemia is a rare and aggressive malignancy, accounting for less than 1% of pediatric leukemias.
2. AML predominates over ALL in neonatal leukemia, and cytogenetic abnormalities, particularly KMT2A (MLL) rearrangements, are common and associated with poor prognosis.
3. Favorable cytogenetic abnormalities are generally associated with higher remission rates than unfavorable rearrangements.
4. Intensive polychemotherapy can achieve high remission rates, but treatment-related toxicity and relapse remain major challenges.

What's new?

1. This study represents one of the first single-center reports from Kazakhstan describing cytogenetic characteristics and treatment outcomes in children with congenital and early infant leukemia.

2. Treatment-related toxicity was markedly more frequent among patients with non-complete remission after induction.

3. The study demonstrates the clinical value of cytogenetic-based risk stratification in a real-world cohort from Kazakhstan.

Limitations

This study has several limitations: its retrospective design, a relatively small patient cohort (n = 33), and the lack of long-term follow-up and supportive therapy data. In addition, a comparative analysis with healthy neonates and older pediatric patients (>6 months) was not performed. These factors may limit the generalizability of the findings and highlight the need for validation in larger, multicenter cohorts.

This investigation represents one of the first single-center reports from Kazakhstan describing congenital acute leukemia in children. It provides valuable insights not only into the clinical and laboratory features and treatment outcomes, but also into key prognostic factors, contributing to the improvement of diagnostic accuracy and therapeutic management of this severe and rare pediatric malignancy.

Conclusion

Congenital acute leukemia (CAL) in children is characterized by early onset, marked clinico-cytogenetic heterogeneity, and variable disease progression. The implementation of risk-adapted chemotherapy based on the cytogenetic profile, together with systematic toxicity monitoring and timely management of complications, enables the achievement of remission in the majority of cases. Further large-scale studies with long-term follow-up are essential to refine prognostic models and to develop national clinical guidelines for the optimal management of this challenging patient population.

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