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RISK FACTORS AND EARLY SIGNS OF CRITICAL CONDITIONS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA ADMITTED TO THE INTENSIVE CARE UNIT

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ABSTRACT

Relevance: *Acute lymphoblastic leukemia (ALL) is the most common cancer among children, accounting for nearly a quarter of all childhood cancers.*

The study aimed to *determine the risk factors and signs of critical conditions in children with acute lymphoblastic leukemia admitted to an intensive care unit (ICU).*

Methods: *The approach used was a systematic review. Data was collected from sources published in 2019-2023. Four cohort studies, four retrospective analyses, two literature reviews, one case-control study, and one case study were included in this systematic review.*

Results: *The prognosis in pediatric ALL depends on the initial number of blast cells in the peripheral blood. Patients with B-cell precursor acute lymphoblastic leukemia (BCP ALL) and low blast cell numbers survived better than patients with T-cell acute lymphoblastic leukemia (T-ALL) and low cell count. IL1B and NLRP1 genetic polymorphisms enhanced ALL risk and reduced infectious comorbidity. However, these gene polymorphisms must be confirmed in juvenile leukemia. KRAS, FLT3, NRAS, PTPN11, KMT2D, PTEN, and NOTCH1 gene mutations affected pediatric ALL patient features and treatment results. These mutations demonstrate the relevance of genetic profiling in risk classification and tailored management. Gene variations and availability of effective medication contributed. Pediatric BCP-ALL patients with the PAX5P80R mutation had worse 5-year overall survival, higher white blood cell counts, male preponderance, and more genetic abnormalities. Pediatric BCP-ALL focused on genetic analysis and risk stratification. Children of African American and European American ancestry showed varied incidence, recurrence, and outcome rates for ALL. African American children exhibited lower incidence but greater recurrence rates and poorer prognosis than European American children.*

Conclusion: *Risk factors for these patients' admission to ICU include comorbidities, infectious diseases, hypoxia, and hemodynamic instability, as well as age and baseline white blood cell count at diagnosis.*

Keywords: *Clinical deterioration, signs of critical conditions, intensive care unit (ICU), acute lymphoblastic leukemia (ALL), children.*

Introduction: Acute lymphoblastic leukemia (ALL) is the most common cancer among children, accounting for nearly a quarter of all childhood cancers [1].

More than 6,600 new cases were diagnosed in the United States in 2022, and nearly 1,600 people died from ALL. Children make up about 60% of all cases, with the highest incidence rate occurring between the ages of two and five. A second peak in incidence comes beyond the age of fifty. Most childhood cancers and 75% of leukemia diagnoses in children below 15 years are ALLs. It ranks behind only accidents as the second-leading cause of death for children under 15 years. After reaching its mid-20s low, the risk progressively starts to grow again. This process continues until age 50. About 20% of adult acute leukemias are caused by ALL. For both sexes, the lifetime risk of ALL is around 0.1% (1 in 1000 Americans). Even though the overall survival rate for children with ALL has significantly increased over the last several decades, some kids still need to be brought to the critical care unit because of a decline in their clinical condition. This is the case even though the overall survival rate for children has significantly improved. Identifying signs or early warning indicators of severe conditions in children with ALL admitted to an intensive care unit (ICU) is vital for improving outcomes and reducing morbidity and mortality rates. It has been shown that the following criteria are both clinically and physiologically important predictors of prognosis in pediatric ALL: age, initial white blood cell count, leukemic blast genetics and immunophenotype, and treatment response.

It is significant to emphasize that over 80% of children with cancer live in LMICs, where treatment results are not optimum. This is mostly brought on by factors that lead to higher treatment-related mortality rates, such as delayed presentation, malnutrition, and a lack of supporting and critical care facilities. A high desertion rate further decreases the survival rates in LMICs. Anemia, thrombocytopenia, and neutropenia are common signs of bone marrow loss in children with ALL, along with visceromegaly and lymphadenopathy [2]. For severely sick patients, the ICU offers extensive monitoring and treatment. Children with ALL admitted to ICU often have a variety of clinical symptoms, such as organ failure, sepsis, respiratory distress, and fever. The underlying causes of clinical deterioration in these cases can vary widely, such as infectious complications, chemotherapy-related toxicities, or organ involvement by leukemia itself [2].

The diagnosis, therapy, and supplementary care of patients with malignancies of the blood have made significant strides over the last several decades, increasing survival rates. However, it is not yet known what the outcome will be for hematologic cancer patients who need admission to the critical care unit. According to recent statistics, these patients' in-hospital death rates vary from 46% to 90%. This is significantly higher than the mortality rates in general medical patients admitted to the ICU over the same period. Through a multivariable analysis, six factors are significant predictors of ICU admission. These factors relate to the patient's health, such as acute leukemia and curative intent chemotherapy, to the patient's laboratory results, such as a platelet count below 50 109/L, albumin levels below normal, and elevated LDH at the time of admission, and to the patient's doctor, such as discussions about advanced directives. These indicators are paramount and may aid healthcare personnel in starting timely and thorough dialogues with patients about treatment objectives, enabling proactive choices before the patient's health deteriorates. It is essential to remember that most patients diagnosed with hematologic cancers will need admission to ICU at some point during treatment. This highlights the significance of using the found predictors to enable efficient discussion with patients about their treatment choices [3].

Detecting early signs of impending clinical deterioration is crucial for timely intervention and improving outcomes in this vulnerable population. Identifying predictors or early harbingers of critical conditions in children with ALL admitted to the ICU is paramount. It allows healthcare providers to recognize subtle changes and initiate appropriate management strategies promptly. However, recognizing these predictors can be challenging, especially in the pediatric population, where symptoms can be nonspecific, rapidly evolving, and influenced by the child's age and developmental stage.

The study aimed to determine the signs in children hospitalized in the critical care unit with acute lymphoblastic leukemia.

Materials and Methods: For this systematic review of early signs of critical conditions in children with ALL admitted to ICU, the data was collected from sources published in 2019-2023. To conduct a PubMed search for early signs of critical conditions in children with ALL admitted to ICU, we use the keywords ("prognosis" AND "pediatric ALL"). Four years: There are 115 articles identified within a specific four-year timeframe. It implies that the search was conducted with a focus on a particular period or interval. Free full: Out of the total results, 66 articles are marked as "free full." This indicates that these articles can be accessed without payment or subscription restrictions. Selected: The dataset includes 17 articles marked as "selected." These articles were reviewed or curated to identify the most relevant and high-quality data. 12 of 295 articles were considered relevant (Fig. 1).

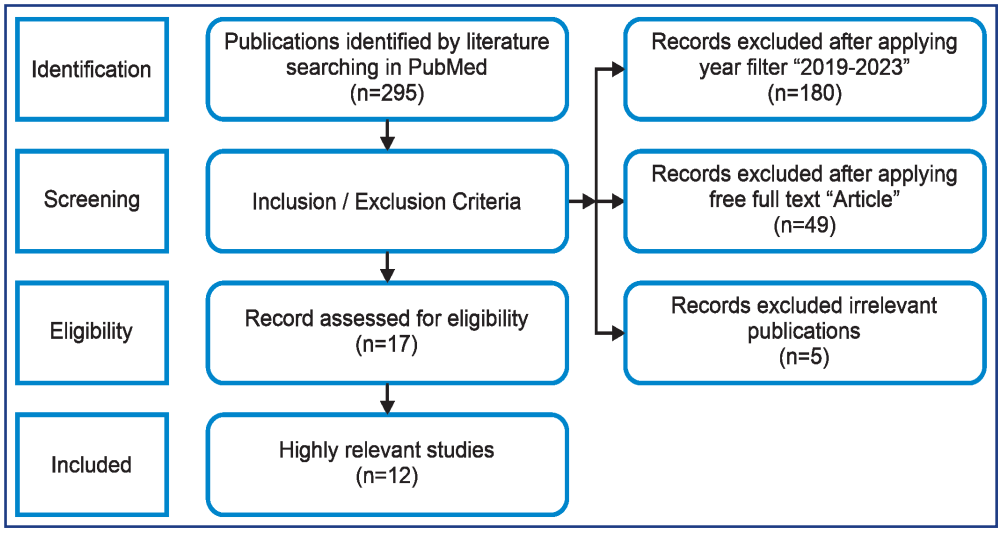

Figure 1 – A Four-Phase Literature Review Flow Diagram

The inclusion and exclusion criteria were:

1. Time Frame: The search was limited to a specific four-year period, possibly to focus on recent developments or to align with a particular study timeline.

2. Availability: "Free full" articles were preferred to open-access materials freely accessible without paywalls or subscription requirements to ensure broader access to the selected articles.

3. Manual Selection: 17 articles were manually selected for a more targeted review. Then, they were scrutinized to identify those of higher quality and relevance.

4. Relevance: Finally, 12 articles were considered relevant, meaning they were especially important or coincident with the research objectives.

Results: According to Table 1, a retrospective cohort study by Dai Q. et al. involved 367 patients with ALL aged 0 to 14 years [4]. F.S. Alves et al. conducted a case-control study involving 158 patients with ALL and 192 healthy individuals aged 2 to 15 years [5]. D. Shen et al. conducted a single-center cohort study with 219 patients diagnosed with pediatric ALL, ranging in age from 0.05 to 16.25 years, with a median age of 3.75 years [6]. W. Burke et al. performed a literature-based evaluation without specifying a sample size, focusing on individuals up to 15 years [7]. M. Jung et al. conducted a retrospective analysis involving 1237 patients with B-cell precursor ALL (BCP-ALL) over ten years [8]. J. Chu et al. conducted a retrospective analysis involving a large

sample of 5,161 children diagnosed with ALL, covering the age range of up to 18 years [9]. A.L. Brown et al. designed a prospective cohort study involving 208 pediatric patients with ALL, aged between 2 and 18 years [10]. F. Liu et al. conducted a retrospective analysis involving 178 patients with ALL, ranging in age from 1 to 13 years [11]. L. Küpfer et al. performed a retrospective analysis involving 110 unselected pediatric patients without specifying the age range [12]. J.T. Nearing et al. conducted a combined 16S rRNA gene and metagenomic shotgun sequencing study in an independent pediatric ALL cohort without providing a specific sample size [13]. A. Kashef et al. conducted a case study involving 241 observations of patients with ALL, ranging in age from 0 to 17 years [14]. Q. Zou et al. performed a literature review and analysis of existing studies, collecting 44 samples from individuals between 0.75 and 11.12 years of age [15].

Table 1 – Overview of study characteristics

Sr. No	Study	Study Design	Sample Size	Age Range
1	Dai Q. et al. [4]	Retrospective Cohort Study	367 patients with ALL	0 to 14 years
2	Alves F.S. et al. [5]	Case-Control Study	192 healthy and 158 ALL patients	2 to 15 years old
3	Shen D. et al. [6]	Single-Center Cohort Study	219 patients with pediatric ALL	0.05-16.25, median: 3.75 years
4	Burke W. et al. [7]	Literature-based evaluation	Not applicable	Up to 15
5	Jung M. et al. [8]	Retrospective analysis	1237 patients with BCP-ALL	Ten years
6	Chu J. et al. [9]	Retrospective analysis	5,161 children with ALL	Up to 18
7	Brown A.L. et al. [10]	Prospective cohort design	208 pediatric patients with ALL	2-18 years.
8	Liu F. et al. [11]	Retrospective analysis	178 patients	1-13 years
9	Küpfer L. et al. [12]	Retrospective analysis	110 unselected pediatric patients	Not specified.
10	Nearing J.T. et al. [13]	Cohort Study	An independent pediatric ALL cohort	Not specified
11	Kashef A. et al. [14]	Case study	241 observations	0 to 17 years
12	Zou Q. et al. [15]	Literature review	44 samples were collected	0.75-11.12 years of age

Early Signs of ALL

Table 2 of the systematic review examined a range of sign variables concerning pediatric ALL. Q. Dai et al. focused on the initial peripheral blood blast cell count at diagnosis [4]. F.S. Alves et al. investigated genetic polymorphisms, including IL1B and IL18, NLRP1, NLRP3, and P2RX7, genotyped using PCR-RFLP and qPCR [5]. D. Shen et al. utilized targeted sequencing through Next-generation sequencing (NGS) to identify gene mutations [6]. W. Burke et al. explored signs such as ALL incidence, relapse rates, prognostic indicators, environmental risk exposures, gene variants associated with treatment response, and access to treatment [7]. M. Jung et al. examined signs, including PAX5P80R status, white blood cell counts, sex, and copy number variations (CNVs) of IKZF1, PAX5, ETV6, RB1, BTG1, EBF1, CDKN2A, CDKN2B, and ERG [8]. J. Chu et al. assessed the response to dexamethasone, categorizing patients into dexamethasone good response (DGR) and dexamethasone poor response (DPR) groups based on peripheral lymphoblast count [9]. A.L. Brown et al. investigated patient-reported symptoms such as fatigue, pain, sleep disruptions, and nausea using surveys completed by patients or caregivers [10]. F. Liu et al. analyzed predictors, including the ETV6-RUNX1 fusion gene, CNS state at diagnosis, prednisolone response, risk level, gene positivity after induction chemotherapy, minimal residual disease (MRD) positivity, and gene positivity at the 12th week [11]. L. Küpfer et al. examined the impact of treatment with a reduced intensity ALL-Moscow Berlin (MB)-91 protocol [12]. J.T. Nearing et al. focused on the gut microbiome composition and its association with infectious complications during the initial six months of therapy [13]. A. Kashef et al. conducted an extensive analysis involving 31 attributes as potential signs in pediatric ALL [14]. Q. Zou et al. investigated genetic mutations (NOTCH1/FBXW7, PTEN, RAS, and KMT2D) and abnormal activation of the JAK-STAT signaling pathway as potential signs in ALL [15]. These studies contribute to understanding the diverse factors that may influence the development, prognosis, and treatment response of pediatric ALL.

Table 2 – Study Early Signs of ALL

Sr. No	Study	Sign Variables
1	Dai Q. et al. [4]	Initial peripheral blood blast cell count at diagnosis
2	Alves F.S. et al. [5]	IL1B and IL18 genetic polymorphisms (genotyped by PCR-RFLP), NLRP1, NLRP3, and P2RX7 genetic polymorphisms (genotyped using qPCR)
3	Shen D. et al. [6]	Gene mutations identified through targeted sequencing based on Next-generation sequencing (NGS)
4	Burke W. et al. [7]	ALL incidence, relapse rates, prognostic indicators, environmental risk exposures, gene variants associated with treatment response, access to treatment
5	Jung M. et al. [8]	PAX5P80R status, white blood cell counts, sex, copy number variations (CNVs) of IKZF1, PAX5, ETV6, RB1, BTG1, EBF1, CDKN2A, CDKN2B, and ERG
6	Chu J. et al. [9]	Response to dexamethasone (classified as dexamethasone good response [DGR] and dexamethasone poor response [DPR] groups based on peripheral lymphoblast count)
7	Brown A.L. et al. [10]	The signs variables were patient-reported symptoms, including fatigue, pain, sleep disruptions, and nausea. The patients or their primary caregivers completed symptom surveys at specific time points during the treatment
8	Liu F. et al. [11]	ETV6-RUNX1 fusion gene, Central nervous system (CNS) state at diagnosis, Prednisone response, Risk level, Gene positivity after induction chemotherapy, Minimal residual disease (MRD) positivity, Gene positivity at the 12th week

Table 2 (continued)

9	Küpfer L. et al. [12]	Treatment with a reduced intensity ALL-Moscow Berlin (MB)-91 protocol
10	Nearing J.T. et al. [13]	Gut microbiome composition, infectious complications during the first six months of therapy
11	Kashef A. et al. [14]	31 attributes
12	Zou Q. et al. [15]	Genetic mutations (NOTCH1/FBXW7, PTEN, RAS, and KMT2D), abnormal activation of signaling pathways (JAK-STAT pathway)

Table 3 summarizes important findings regarding pediatric ALL. Q. Dai et al. found that the initial peripheral blood blast cell count influenced the clinical prognosis of pediatric ALL. Specifically, patients with B-cell precursor acute lymphoblastic leukemia (BCP ALL) and low blast cell counts had better survival rates, while those with T-ALL and low counts had worse survival rates than intermediate and high counts [4]. F.S. Alves et al. focused on inflammasome gene polymorphisms and their association with ALL risk and infectious comorbidities. They discovered that certain genetic variants, such as IL1B and NLRP1, were linked to an increased risk of ALL and decreased susceptibility to infectious comorbidities. However, larger-scale investigations are required to validate the significance of these gene polymorphisms in juvenile leukemia [5]. D. Shen et al. identified 381 mutations in 66 different genes in pediatric ALL patients. They found that specific mutations, including KRAS, FLT3, NRAS, PTPN11, KMT2D, PTEN, and NOTCH1, were associated with particular patient characteristics and treatment outcomes. This highlights the importance of genetic mutations in risk stratification and personalized management of ALL [6]. W. Burke et al. investigated the disparities in ALL incidence, relapse rates, and prognostic markers between African American (AA) and European American (EA) children. They discovered that AA children had lower incidence but higher relapse rates and worse prognostic markers than EA children. Environmental risk factors had a limited impact, while gene variations and differential access to effective therapy contributed to these disparities. Precision medicine was suggested as a potential solution to address these gaps [7]. M. Jung et al. examined the presence of the PAX5P80R mutation in pediatric BCP-ALL patients and its impact on clinical outcomes. They found that patients with this mutation had worse 5-year overall survival, higher white blood cell counts, male predominance, and additional genetic abnormalities. This highlights the importance of genetic profiling and risk stratification in pediatric BCP-ALL [8]. J. Chu et al. focused on the response to dexamethasone as a prognostic factor in pediatric ALL. Based on the peripheral lymphoblast count, they divided the patients into groups for dexamethasone's excellent reaction and dexamethasone's poor response. DPR patients had higher relapse rates and lower 6-year event-free survival and overall survival rates, emphasizing the importance of early therapeutic response assessment and tailored management [9]. A.L. Brown et al. investigated the association between patient-reported symptoms and the incidence of relapse in pediatric ALL. They discovered that certain symptoms at various stages of treatment – such as weariness, discomfort, disturbed sleep, and nausea, were connected to an elevated chance of recurrence. Symptom clusters and higher symptom load were also associated with recurrence [10]. F. Liu et al. evaluated the prognostic factors and treatment outcomes in pediatric ALL. They reported favorable outcomes in ETV6-RUNX1-positive patients but highlighted the need to carefully consider CNS involvement and minimal residual disease levels for appropriate treatment decisions [11]. L. Küpfer et al. studied the outcomes of reduced-intensity ALL-MB-91 treatment in pediatric ALL patients. They found a 3-year event-free survival rate of 34.9% and suggested that tailored treatment intensity and improved platelet infusion might enhance outcomes [12]. J.T. Nearing et al. explored the relationship between gut microbiota composition and infectious complications in pediatric ALL patients during treatment. They discovered that specific gut microbiome characteristics were associated with increased vulnerability to viral problems, highlighting the potential role of the microbiome in patient outcomes [13]. A. Kashef et al. examined the necessity of cranial radiotherapy (CRT) in pediatric ALL patients and developed a classifier to predict the need for CRT based on disease recurrence. They found that CRT was cost-effective and beneficial for patients with a higher risk of recurrence [14]. Q. Zou et al. reviewed prognostic factors, genetic and molecular characteristics, and optimal treatment modalities in adult T-LBL. They emphasized the importance of genetic mutations, such as NOTCH1/FBXW7, PTEN, RAS, and KMT2D, and abnormal signaling pathways, particularly the JAK-STAT pathway. The study recommended specific treatment approaches while considering the benefits and risks of radiotherapy and highlighted the significance of prognostic models in guiding therapy selection [15].

Table 3 – Main results of the studies included in the analysis

Sr. No	Study	Outcome Measure	Results	Findings
1	Dai Q. et al. [4]	The clinical prognosis of pediatric ALL	BCP ALL was 91.6%, T-ALL 8.4%. BCP ALL and T-ALL patients' prognoses depended on their initial peripheral blood blast cell count	BCP ALL patients with low blast cell counts (<1×10^9/L) showed better survival rates than those with large counts (>30×10^9/L). T-ALL patients with low counts had worse survival rates than intermediate counts (1-29.9×10^9/L) and high counts

Table 3 (continued)

2	Alves F.S. et al. [5]	Inflammasome gene polymorphisms and ALL and infectious comorbidities	IL1B C/T rs19644 genotype increases ALL risk by 2.48-fold, whereas NLRP1 A/T rs12150220 genotype decreases infectious comorbidities by 0.37-fold. NLRP3 and P2RX7 polymorphisms did not affect risk	Larger-scale investigations are needed to validate the relevance of inflammasome gene polymorphisms in juvenile leukemia.
3	Shen D. et al. [6]	Patient characteristics, cytogenetics, genetic subtypes, risk stratification, and treatment results are correlated with gene mutation	381 gene mutations were identified in 66 different genes in 152/219 patients	KRAS, FLT3, NRAS, PTPN11, KMT2D, PTEN, and NOTCH1 mutations were related to particular patient features (P<0.050). PIK3R1 mutation was more common in babies (P=0.021). ETV6 and PHF6 mutations lowered steroid sensitivity (P=0.033 and 0.048, respectively)
4	Burke W. et al. [7]	ALL disparities between African American (AA) and European American (EA) children	AA children had a lower ALL incidence but greater recurrence rates and worse prognostic markers than EA children. Due to limited evidence, environmental risk factors for ALL had little effect, although treatment response gene variations increase AA children's recurrence rates. Risk-directed treatment, case management, and no out-of-pocket payments may reduce ALL recurrence rates	AA children had lower incidence, greater relapse rates, and worse prognoses than EA children. Due to insufficient data, environmental risk exposures on ALL are unknown, whereas gene variations and differential access to effective therapy contribute to the reported discrepancies. Precision medicine may address these gaps by personalizing treatment techniques for varied patient groups
5	Jung M. et al. [8]	5-year overall survival	PAX5P80R was detected in 2% of BCP-ALL patients, with greater white blood cell counts and male sex. Most PAX5P80R-positive individuals were ≥10 years old and had PAX5, IKZF1, CDKN2A, and CDKN2B deletions, leading to lower 5-year overall survival than in PAX5P80R-wildtype BCP-ALL	Pediatric BCP-ALL patients treated with the AIEOP-BFM ALL 2000 regimen who had PAX5P80R had worse clinical results, including poorer 5-year overall survival. PAX5P80R's association with other genetic abnormalities and intermediate-risk pediatric BCP-ALL risk classification requires more study
6	Chu J. et al. [9]	The prognosis (recurrence rate, 6-year event-free survival, and overall survival rates)	Compared to DGR, DPR had greater age, white blood cell counts, BCR/ABL1 and TCF3/PBX1 fusion genes frequency, and central nervous system recurrence (P<0.001). The DGR group had reduced recurrence rates (18.6% vs. 11%) and greater 6-year event-free survival (73% vs. 83%) and overall survival (86% vs. 92%). Only the intermediate-risk group differed (P<0.001)	Dexamethasone caused an early therapeutic response. Dexamethasone response and low residual disease were prognostic in the intermediate-risk group, possibly directing early management to minimize recurrence
7	Brown A.L. et al. [10]	The main outcome measure was the incidence of relapse in pediatric ALL patients	A total of 208 patients were followed up for a mean period of 2.6 years. A relapse occurred in 22 patients	The research found substantial connections between recurrence and certain symptoms at different treatment phases. Fatigue at the onset of delayed intensification (DI) and maintenance cycle 1 (MC1), pain at DI, nausea after induction, and sleep problems at the end of induction, DI, and MC1 all increased relapse risk. Symptom clusters with greater average DI symptom load were also related to recurrence
8	Liu F. et al. [11]	The induced remission rate, cumulative relapse incidence, 5-year and 10-year OS/EFS rates, and related prognostic variables affect medical research results	The median white blood cell count at diagnosis was 9.46×10^9/L, and the median age was 4 years. The initial induction treatment achieved a 97.8% remission rate, while 15.9% of patients relapsed, predominantly as isolated bone marrow relapse (83.3%) and late relapses (79.2%). The median relapse to first full remission was 35.5 months. ETV6-RUNX1-positive children had 5-year and predicted 10-year overall survival rates of 89.4% and 88.6% and event-free survival rates of 82.1% and 77.3%	ETV6-RUNX1-positive ALL has a good prognosis, although individuals with CNS2 at diagnosis or high MRD levels at 12 weeks should have stem cell transplantation

Table 3 (continued)

9	Küpfer L. et al. [12]	Event-free survival (EFS) and overall survival (OS)	No patients stopped therapy, and 57% were high-risk. 65.5% obtained full remission on day 36. The 3-year event-free survival (EFS) and overall survival (OS) rate was 34.9%, with infections (53.3%) and bleeding (20%) causing the most fatalities. Standard-risk (SR) individuals had 50.5% 3-year EFS	The lower intensity ALL-MB-91 treatment in a charity-funded public hospital in Cambodia had a 3-year event-free survival rate of 34.9% for pediatric ALL patients. Infections and bleeding killed most. The research also implies that leukemia treatment may be justified with selective lowering of treatment intensity and enhanced platelet infusion
10	Nearing J.T. et al. [13]	Gut microbiota composition and pediatric ALL infectious complications	Infectious problems within six months of medication were associated with unique gut microbiota alpha diversity, beta diversity, species abundance, and functional pathways. These results show that the gut microbiome's makeup and activity determine patients' vulnerability to viral problems during treatment	This research examines the gut microbiota and infectious problems in pediatric ALL patients following therapy. The findings emphasize taxonomic and functional microbiome differences. Machine learning models employing patient information and bacterial species had an 84.09% classification accuracy. Bacterial species were the most relevant characteristics. This connection and its implications for future research and therapeutic practice need more study
11	Kashef A. et al. [14]	The necessity of Cranial Radiotherapy (CRT) treatment in pediatric ALL patients	The stacked ensemble classifier used in the study demonstrated highly reasonable performance with an Area Under the Curve (AUC) of 87.52%	In pediatric ALL patients, disease recurrence is the main predictor of CRT therapy, which is cost-effective and beneficial
12	Zou Q. et al. [15]	Prognostic factors, genetic and molecular characteristics, optimal treatment modalities	Genetic mutations (NOTCH1/FBXW7, PTEN, RAS, KMT2D) and aberrant JAK-STAT signaling were studied in adult T-LBL. Leukemia treatment, CNS prophylaxis, and cranial radiation-free procedures were used. 5-miRNA, 11-gene, and 4-CpG classifiers predicted outcomes	The review study covered adult T-LBL's genetic and molecular features, recommended treatment options, and emphasized the significance of genetic mutations and abnormal signaling pathways. It also highlighted the importance of prognostic models and recommended specific therapies while considering the benefits and risks of radiotherapy

Discussion: This systematic review on Early Signs and risk factors of Critical Conditions in Children with ALL Admitted to ICU includes 4 cohort studies, 4 retrospective analyses, 2 literature reviews, 1 case-control study, and 1 case study.

Different research discovered that several clinical and laboratory prognostic markers utilized for B-precursor ALL were much less predictive in T-ALL; other criteria, such as the time to relapse and the relapse location, were significant prognostic factors for survival [16]. A separate study has also shown that ALL children below 15 years have a very good prognosis, with cure rates exceeding 85%. However, the prognosis for ALL grows less promising as people age. In the past, only 30% to 40% of individuals over 40 years were cured. Relapsed ALL continues to cause cancer-related deaths in people of all ages [17].

The systematic review of the original question focuses on various sign variables; the search results cover a broader range of topics related to ALL. Regular laboratory tests for pediatric ALL include lumbar puncture, bone marrow aspiration and biopsy, complete blood count, and peripheral blood smear [18]. Overall, the search results provide a more comprehensive understanding of the diagnosis, treatment, and prognosis of pediatric ALL, including the use of risk-adapted treatment protocols and the importance of genetic and molecular factors in determining prognosis. This systematic review focuses on signs of critical conditions in pediatric ALL, including initial peripheral blood blast cell count, genetic polymorphisms, gene mutations, prognostic indicators, treatment response, and access to treatment. Other literature from 2019 to 2023 provides additional insights into prognostic factors, treatment outcomes, genetic and molecular characteristics, and disparities in ALL. Pharmacological heterogeneity of ALL exists, and drug response varies across molecular subtypes [19]. Patient-reported symptoms such as fatigue, pain, sleep disruptions, and nausea are associated with the incidence of relapse in pediatric ALL. The gut microbiome composition is associated with infectious complications during ALL treatments. Genetic mutations and abnormal activation of signaling pathways play a role in ALL prognosis and treatment responses.

According to a study of pediatric patients, the typical risk factors for ICU admission are the following:

– Infectious and respiratory diseases, comorbidities, acute respiratory distress syndrome [20, 21];

– Hyperleukocytosis, neural leukosis, infections, hemorrhagic syndrome [22];

– Severe course of the underlying disease, hypoxia, inability to eat and drink [23];

– Age, neurologic impairment, chronic disease, and immunodeficiency [24].

These risk factors highlight the importance of monitoring and managing comorbidities, infectious diseas-

es, and respiratory and cardiovascular function in pediatric patients to prevent ICU admission.

The available information describes the primary reasons for patients with ALL admission to ICU. However, comparing these results with other research studies is crucial for a more comprehensive knowledge of the reasons for ICU admissions. The most frequent causes of ICU admission in the United States, according to research published in the BMC Emergency Medicine journal, were chest discomfort, heart failure, and pneumonia [25]. According to the Ottawa Hospital data, cancer patients sometimes require ICU admission for bleeding or infection, usually after chemotherapy or bone marrow transplantation. Overall, the reasons for ICU admission can vary depending on age, sex, type of hospital, and geographic location. However, respiratory issues, cardiac problems, renal issues, and sepsis are common reasons for ICU admission in various studies. Unified approaches to early precursors of critical conditions in children with ALL are required to prevent critical conditions and reduce adverse outcomes of the disease [26].

Conclusion: Based on the data presented, several conclusions can be drawn regarding prognostic factors, signs, and underlying reasons for admission to the ICU of pediatric patients with ALL and hematologic malignancies: age, initial white blood cell count at diagnosis, ALL subtypes, and initial response to treatment are important prognostic factors. However, genetic abnormalities and recurrence are also important for prognosis. Comorbid conditions, infectious diseases, hypoxia, organ dysfunction, etc. are common risk factors for ICU hospitalization. Larger studies show that sepsis, respiratory, cardiac, neurological, and renal diseases are frequent causes of ICU hospitalization. Hematologic malignancies require further examination of prognostic variables and prognosis of ICU admission. This will help to improve the understanding and management of these diseases. Pediatric patients with ALL, especially those at increased risk of ICU admission, require close monitoring and follow-up to address potential complications in due time and reduce the need for intensive care. Healthcare providers should allocate appropriate resources, including trained staff, equipment, and infrastructure, to effectively manage pediatric patients with ALL. This will optimize patient outcomes and reduce the burden on intensive care units.

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АНДАТПА

РЕАНИМАЦИЯ БӨЛІМІНЕ ТҮСКЕН ЖЕДЕЛ ЛИМФОБЛАСТИКАЛЫҚ ЛЕЙКЕМИЯМЕН АУЫРАТЫН БАЛАЛАРДАҒЫ АУЫР ЖАҒДАЙЛАРДЫҢ АЛҒАШҚЫ БЕЛГІЛЕРІ ЖӘНЕ ҚАУІП ФАКТОРЛАРЫ

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Өзектілігі: *Жедел лимфобластикалық лейкоз (ЖЛЛ) балалар арасындағы ең көп таралған қатерлі ісік болып табылады, ол барлық балалар ісіктерінің төрттен бір бөлігін құрайды.*

Зерттеудің мақсаты *– реанимация және қарқынды терапия бөліміне (РҚТБ) түскен жедел лимфобластикалық лейкозбен ауыратын балалардағы қауіп факторлары мен ауыр жағдайдың белгілерін анықтау.*

Әдістері: *Ретінде жүйелі шолу қолданылды. Деректер 2019-2023 жылдары жарияланған дереккөздерден жиналды. Жүйелі шолуға төрт когорттық зерттеу, төрт ретроспективті талдау, екі әдебиетке шолу, бір «жағдайды-бақылау»» зерттеуі және бір жағдайды зерттеу кірді.*

Нәтижелері: *Педиатриялық ЖЛЛ болжамына перифериялық қандағы бласт жасушаларының бастапқы саны әсер етеді. Бласт жасушаларының саны төмен деңгейдегі В-ЖЛЛ пациенттері, төмен деңгейлі Т-ЖЛЛ пациенттеріне қарағанда болжамы жақсы. IL1B және NLRP1 генетикалық полиморфизмдері жедел лимфобластикалық лейкоздың даму қауіпін арттырады және инфекциялық үйлесімділікті төмендетті. Алайда, бұл гендердің полиморфизмдері ювенильді лейкемияда расталуы керек. KRAS, FLT3, NRAS, PTPN11, KMT2D, PTEN және NOTCH1 гендерінің мутациялары педиатриялық ЖЛЛ бар науқастардың сипаттамалары мен нәтижелеріне әсер етті. Бұл мутациялар қауіп қатерді жіктеу және емдеуді даралау үшін генетикалық профильдеудің өзектілігін көрсетеді. Бұған гендік вариация және тиімді дәрі-дәрмектердің болуы ықпал етті. PAX5P80R мутациясы бар емделушілерде 5 жылдық жалпы өмір сүру ұзақтығы төмен, лейкоцит клеткаларының деңгейі жоғары, ерлерде басым және генетикалық ауытқулар көп болды. Педиатриялық В-ЖЛЛ генетикалық талдау мен қауіп қатерді стратификациялауға бағытталған. Афроамерикалық (АА) және еуроамерикалық (ЕА) тектес балаларда ЖЛЛ ауруының, қайталануының және нәтижелерінің әртүрлі көрсеткіштері байқалды. АА балаларының жиілігі төмен, бірақ қайталану жиілігі жоғары және болжам ЕА балаларына қарағанда нашар.*

Қорытынды: *Осы науқастардың реанимация бөліміне жатқызылу қауіп факторлары қатар жүретін аурулар, жұқпалы аурулар, гипоксия және гемодинамикалық тұрақсыздық, сондай-ақ диагноз кезінде жасы мен лейкоциттер санының бастапқы көрсеткіштері болып табылады.*

Түйінді сөздер: *Клиникалық нашарлау, критикалық жағдайлардың белгілері, қарқынды емдеу бөлімшесі (ҚЕБ), жедел лимфобластикалық лейкемия (ЖЛЛ), балалар.*

АННОТАЦИЯ

ФАКТОРЫ РИСКА И РАННИЕ ПРИЗНАКИ КРИТИЧЕСКИХ СОСТОЯНИЙ У ДЕТЕЙ С ОСТРЫМ ЛИМФОБЛАСТНЫМ ЛЕЙКОЗОМ, ПОСТУПИВШИХ В ОТДЕЛЕНИЕ ИНТЕНСИВНОЙ ТЕРАПИИ

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Актуальность: *Острый лимфобластный лейкоз (ОЛЛ) – наиболее распространенное онкологическое заболевание среди детей, составляющее почти четверть всех детских онкологических заболеваний.*

Цель исследования *– определить факторы риска и признаки критических состояний у детей с острым лимфобластным лейкозом, поступивших в отделение реанимации и интенсивной терапии (ОРИТ)*

Методы: *В качестве подхода использовался систематический обзор. Данные были собраны из источников, опубликованных в 2019-2023 гг. В систематический обзор были включены четыре когортных исследования, четыре ретроспективных анализа, два обзора литературы, одно исследование типа «случай-контроль» и одно исследование случая.*

Результаты: *Прогноз при педиатрическом ОЛЛ зависит от исходного количества бластных клеток в периферической крови. Больные с В-ОЛЛ и низким количеством бластных клеток выживали лучше, чем больные с Т-ОЛЛ с низким числом клеток. Генетические полиморфизмы IL1B и NLRP1 повышали риск развития ОЛЛ и снижали инфекционную коморбидность. Однако полиморфизмы этих генов должны быть подтверждены при ювенильном лейкозе. Мутации генов KRAS, FLT3, NRAS, PTPN11, KMT2D, PTEN и NOTCH1 повлияли на характеристики и результаты лечения пациентов с педиатрическим ОЛЛ. Эти мутации демонстрируют актуальность генетического профилирования для классификации риска и индивидуализации лечения. Этому способствовали генные вариации и доступность эффективных лекарственных препаратов. Пациенты с педиатрическим В-ОЛЛ с мутацией PAX5P80R имели худшую 5-летнюю общую выживаемость, более высокий уровень лейкоцитов, преобладали мужчины и имели больше генетических аномалий. При педиатрическом В-ОЛЛ основное внимание уделяется генетическому анализу и стратификации риска. У детей афроамериканского (АА) и евро-американского (ЕА) происхождения наблюдались различные показатели заболеваемости, рецидивов и исходов ОЛЛ. У детей АА заболеваемость ниже, но частота рецидивов выше, а прогноз хуже, чем у детей ЕА.*

Заключение: *Факторами риска госпитализации в отделение интенсивной терапии у таких пациентов являются сопутствующие заболевания, инфекционные болезни, гипоксия и гемодинамическая нестабильность, а также возраст и исходное количество лейкоцитов в крови при постановке диагноза.*

Ключевые слова: *клиническое ухудшение, признаки критических состояний, отделение интенсивной терапии (ОИТ), острый лимфобластный лейкоз (ОЛЛ), дети.*

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