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Hospitalization in the Intensive Care Unit of Children with Acute Lymphoblastic Leukemia: A Retrospective Cohort Study

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Abstract

Background: To examine how sociodemographic factors like age, gender, ethnicity, and socioeconomic status relate to early precursors of ALL (acute lymphoblastic leukemia), evaluate their distribution among Acute Lymphoblastic Leukemia (ALL) variants, FAB (French-American-British) classification, and comorbidities, and explore associated clinical profiles. Then, assess their significance on therapy outcomes in ICU (intensive care unit) settings.

Methods: A retrospective cohort study investigated the association between early detection of critical condition precursors and outcomes in pediatric ALL patients. Data from 188 ICU-admitted children were analyzed, exploring sociodemographic, clinical factors, and ICU outcomes, using SPSS for statistical analysis. Statistical methods included chi-square tests for categorical variables, independent sample t-tests for continuous variables, and multivariate logistic regression to identify prognostic factors influencing ICU outcomes.

Results: The study on ICU hospitalization of children with ALL revealed several important findings. Of 188 children admitted to the ICU, 98 (52.1%) were aged 8-18 years and 97 (51.6%) were male. Most participants had a weight ≤30 kg (56.9%) and reduced BMI (63.3%). The common ALL variant was most frequent (76, 40.4%). During ICU stay, 50 patients (26.6%) died and 138 (73.4%) were transferred to specialized oncology care. During the study period, 165 (87.8%) patients had a single ICU admission, while 23 (12.2%) experienced two or more ICU admissions. Male patients were more often transferred to oncology care (80/97, 82.5%; P=0.004). Mortality was significantly higher among those with reduced BMI (26/69, 37.7%; P=0.009) and concomitant diseases (15/33, 45.5%; *P*=0.007). Logistic regression identified male gender (Exp(B)=3.031, P=0.003) and concomitant diseases (Exp(B)=2.538, P=0.033) as significant predictors of adverse outcomes. Re-hospitalization frequency was associated with higher weight (mean 48.9 ± 23.3 kg vs. 27.7 ± 16.2 kg, *P*<0.001).

Conclusion: This study identified key prognostic factors in pediatric ALL patients in the ICU, including gender, concomitant diseases, BMI, relapse, and risk group. These factors significantly influenced mortality and re-hospitalization rates, underscoring the importance of tailored management strategies for improved outcomes.

Keywords: Early Detection, Precursors, Critical Condition, Acute Lymphoblastic Leukemia, Pediatrics

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↑What is "already known" in this topic:
Pediatric patients with Acute Lymphoblastic Leukemia often require admission to the intensive care unit due to treatment complications, comorbidities, or critical illness. Previous research has highlighted the role of sociodemographic and clinical factors in influencing survival and treatment outcomes in ALL, but evidence specifically focused on ICU settings remains limited. Key risk factors such as gender, nutritional status, and comorbid conditions have been linked to poorer outcomes in pediatric oncology, yet their prognostic value in ICU-admitted ALL patients has not been well defined.

→What this article adds:
This study identifies gender, chronic diseases, body mass index, relapse, and risk group as significant prognostic factors for mortality and re-hospitalization in pediatric ALL patients admitted to the ICU. It provides new evidence that male gender and chronic disease independently predict adverse ICU outcomes, with BMI also strongly influencing mortality. By clarifying these prognostic factors, the study supports the development of early detection strategies, individualized care approaches, and resource prioritization for high-risk groups in pediatric intensive care settings.

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Introduction

leukocytes and bone marrow, leading to the overproduction of immature lymphoid cells, called leukemic cells. This proliferation results in the replacement of healthy hematopoietic cells, causing complications such as infections, anemia, and excessive bleeding (1). While ALL can occur across all age groups, it is most common in children aged 1-4 years. The disease is often associated with genetic predispositions and environmental exposures, though these factors are detected in only a few cases. Chromosomal abnormalities and genetic alterations contribute to the formation and proliferation of lymphoid precursor cells, driving the disease's progression. The prognosis is poorer for older individuals (≥40 years) and those with relapsed or refractory ALL, while children and adolescents show better outcomes with aggressive treatment strategies (2).

In the United States, approximately 6,000 new cases of ALL are diagnosed annually, making it the most common childhood cancer, accounting for 25% of all cancer cases in children. The incidence is highest among children aged 2-5 years, with rates varying by race and ethnicity. The Hispanic population has the highest incidence (40.9 cases per million), followed by the white (35.6) and black populations (14.8). Immunophenotyping categorizes ALL into B-cell (B-ALL), which accounts for 85% of cases, and T-cell (T-ALL), with distribution influenced by age, race, and ethnicity (3).

Recent advances in genetic and molecular research have significantly improved our understanding of ALL's biological and genetic causes, leading to better treatment categorization and experimental models for studying the disease. These developments have enabled improved prognostic assessments and targeted therapeutic approaches (4).

A key tool in managing ALL in pediatric settings is the Pediatric Early Warning Score (PEWS), which assesses clinical deterioration based on behavior, cardiovascular, and respiratory parameters. PEWS facilitates early detection of clinical decline and escalates care, when necessary, which is particularly crucial in high-risk pediatric populations, including those with cancer. Its use in oncology has proven effective in preventing disease progression by enabling timely interventions (5, 6).

However, the treatment of ALL can lead to severe complications such as infections, anemia, thrombocytopenia, and coagulopathies, which require prompt identification and management. These conditions may arise from the disease itself or as side effects of treatments like chemotherapy. Children with ALL are also at increased risk of infections due to the immunosuppressive effects of their treatment. Identifying early signs of these complications is critical for improving outcomes and reducing the risk of severe disease progression (7).

Factors contributing to the onset of severe predisposition for ALL in children include the leukemia subtype, genetic abnormalities specific to this subtype that could increase the risk, and the immature immune systems in infants and toddlers, which may make these children more susceptible to infections. Among the treatment-related factors that increase the risks of infections and toxicities associated with chemotherapy are the intensity and duration of the treatment, as well as the medications used. Socioeconomic status is also an important factor that may affect access to healthcare. Additionally, children with ALL may have other pre-existing medical conditions or genetic disorders, which can exacerbate the severity of complications (8).

Education for parents, nurses, and doctors is crucial to identify early detection methods for critical conditions in children with ALL. Behavioral and cognitive changes in children with ALL may influence timely recognition of clinical deterioration. Changes in platelet counts and related hematologic indices have been associated with severity and prognosis in critically ill pediatric patients, supporting their potential utility as early indicators of critical conditions in the ICU setting (9).

Early diagnosis relies on three key factors: measuring clinical indicators, raising parental awareness, and assessing healthcare providers' attitudes towards the condition. These elements create opportunities for timely interventions, reducing complications, and extending treatment options (10). This study seeks to investigate the relationship between demographic and clinical characteristics, such as age, gender, and BMI, and ICU outcomes in patients with acute lymphoblastic leukemia (ALL). It aims to identify key prognostic factors that significantly influence ICU therapy outcomes and to explore how these factors are associated with the frequency of re-hospitalization during the same admission. Additionally, the study examines the impact of relapse history on the overall outcomes of ALL patients admitted to the ICU.

The main goal of this retrospective cohort study was to identify the key prognostic factors influencing intensive care unit (ICU) outcomes in children with acute lymphoblastic leukemia (ALL).

To achieve this, the study specifically aimed to:

Analyze the relationship between demographic and clinical characteristics (age, gender, BMI, etc.) and ICU outcomes in ALL patients.

Identify the key prognostic factors influencing ICU therapy outcomes in ALL patients.

Examine the association between clinical factors and the frequency of re-hospitalization during the same admission in ALL patients.

Evaluate the impact of relapse history on patient outcomes in ICU-admitted ALL patients.

Methods

A retrospective cohort study was conducted to investigate the relationship between early detection of critical condition precursors and outcomes in children with acute lymphoblastic leukemia (ALL). The study was conducted at the Scientific Center of Pediatrics and Pediatric Surgery (SCPPS; also referred to as NCPDH), a single tertiary-care center treating only its own patients. Data were col-

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lected from January 2020 to December 2022, including all children with ALL admitted to the intensive care unit (ICU) during this period.

Sample Size

The study included all pediatric patients (n = 188) diagnosed with ALL and admitted to the ICU at SCPPS between January 2020 and December 2022. As this was a retrospective study including the entire eligible patient population, no formal sample size calculation was required.

Inclusion and Exclusion Criteria

Children aged up to 18 years diagnosed with ALL and admitted to the ICU at SCPC were included if complete medical records were available for the ICU admission episode. Patients were excluded if they had incomplete medical records, were admitted to the ICU for critical conditions unrelated to ALL or its treatment (e.g., trauma or non-oncologic surgical conditions), or received treatment outside of SCPC.

Patients diagnosed with ALL prior to 2020 were included only if they required ICU admission during the study period and were classified as relapsed or recurrent cases rather than newly diagnosed patients.

Data Collection

Data were gathered from both paper-based and electronic inpatient medical records at SCPC. The following variables were collected:

Demographic characteristics (age, sex)

Clinical characteristics related to ALL

ICU admission characteristics

Early indicators of critical condition (e.g., respiratory distress, hemodynamic instability, laboratory abnormalities, and organ dysfunction)

ICU outcomes (death or transfer to oncology department)

Number of ICU admissions during the study period

Nationality and the year of diagnosis were not treated as independent variable analyses because the study was undertaken in a single country, and earlier diagnoses reflected recurrent occurrences rather than new episodes of the disease.

Data Analysis

Data were analyzed using SPSS 26. Descriptive statistics were calculated, including frequencies and percentages for categorical variables, and means with standard deviations or medians with interquartile ranges for continuous variables. The following statistical methods were employed:

T-test (Independent Samples): This test was used to compare the means of continuous variables (e.g., age, BMI, weight categories) between two independent groups (e.g., patients who developed critical conditions and those who did not develop critical conditions). The t-test was chosen because it is appropriate for comparing the means of normally distributed continuous data between two groups.

Chi-Square Test: This test was used to examine the association between categorical variables and the occurrence of critical conditions. It was chosen because it is useful for testing relationships between categorical variables and determining if differences in proportions are statistically significant. However, when the frequency of any cell in the contingency table was less than 5, the Chi-Square test was not reliable due to the expected count assumptions. In such cases, the Odds Ratio (OR) were calculated to assess the strength of the association between categorical variables and critical outcomes. The OR provides an estimate of the odds that an outcome (e.g., critical condition) occurs in one group relative to another, and it is especially useful when frequencies are low (i.e., <5) and the Chi-Square test assumptions may be violated.

Multivariate Logistic Regression: Used to assess the relationship between multiple predictors (e.g., early detection of critical condition precursors, weight categories, age group) and the likelihood of ICU therapy outcomes (e.g., death, transfer to oncology department). This regression method was chosen to control for potential confounders and effect modifiers.

Survival analysis could not be completed because there were no data available for follow-ups that extend further than the discharge from the Intensive Care Unit. For the sake of maintaining statistical validity and avoiding overstratification, some of the categorical variables were combined. Statistical comparisons involving extremely small subgroups were not performed. A significance level of 0,05 was used for all two-tailed statistical tests.

Results

Table 1 presents the demographic and clinical characteristics of the study population. Variables included age, sex, weight, BMI, ALL variant, FAB classification, heredity, at-risk group, blood type, and Rhesus factor. Most participants were aged 8-18 years (52.1%), and 51.6% were male. A majority had a body weight of ≤30 kg (56.9%), and 63.3% had reduced BMI. The most common ALL subtype was common ALL (40.4%), and FAB L1 was the predominant classification (68.1%). Heredity was unspecified in most cases (97.9%). More than half of the patients were classified as high risk (55.3%). Blood group A (II) was the most frequent (38.3%), and 98.4% had a positive Rhesus factor. All diagnosis year and nationality were omitted from the analysis because the study was single center and earlier diagnosis were recurrent cases rather than new disease onset.

Figure 1 shows that among the cohort of ALL patients admitted to the ICU, 26.6% died during their ICU stay, while the majority, 73.4%, were successfully transferred to specialized oncology departments for continued care. Regarding ICU admission history, 165 (87.8%) patients had a single ICU admission, whereas 23 (12.2%) experienced two or more separate ICU admissions during the study period.

Table 2 a comparative analysis of quantitative prognostic factors among ICU patients based on therapy outcomes using independent sample t test showed no statistically

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Table 1. Demographic and Clinical Profile of Participants with Acute Lymphoblastic Leukemia (ALL)

Variable	Category	No	%	Variable	Category	No	%
Age (years)	0-7	90	47.9	FAB Classification	L1	60	31.9
	8-18	98	52.1		Other (L2, L3)	128	68.1
Gender	Female	91	48.4	Heredity	Not specified	184	97.9
	Male	97	51.6		Maternal side	3	1.6
					Paternal side	1	0.5
				At-risk group	Standard	52	27.7
Weight, Kg	≤ 30	107	56.9		Medium	32	17.0
	31-60	60	31.9		High	104	55.3
	> 60	21	11.2	Blood Type	O(I)	58	30.8
BMI	Reduced	69	36.7		A(II)	72	38.3
	Promoted	119	63.3		B(III)	40	21.3
ALL Variant	Pro-B	36	19.1		AB(IV)	18	9.6
	Pre-B	25	13.3	Rhesus factor	Negative	3	1.6
	common	76	40.4		Positive	185	98.4
	T cortical	36	19.1				
	*Others	15	8.0				
Relapse of the disease	No	126	67.0				
	1 time	43	22.9				
	2 times	19	10.1				

* T noncortical, In mature cell, biphenotypic (B+M))

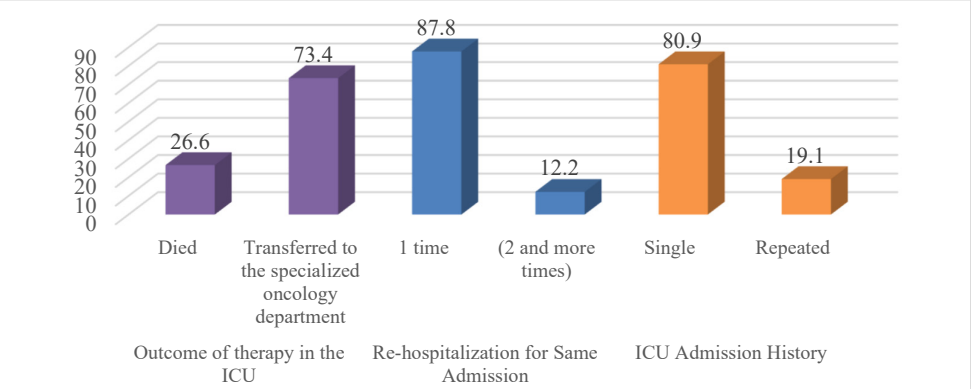

Figure 1. Clinical Outcomes and Admission History in ICU ALL Patients

Table 2. Prognostic Factors and ICU Therapy Outcomes Age and Weight Analysis

Variable	Outcome of therapy in the ICU		t-value (*P*-value)	95% Confidence Interval of the Difference
	Died (n=50) Mean ± SD	Transferred to the specialized oncology department (n=138) Mean ± SD		
Age	8.15 ± 5.16	7.59 ± 5.04	0.67 (0.51)	(-1.09, 2.21)
Weight, kg	32.21 ± 19.7	29.62 ± 18.06	.847 (.398)	(-3.44, 8.61)

significant differences in age or weight between those who died (n=50) and those transferred to specialized oncology departments (n=138). The mean age was slightly higher in the deceased group (8.15 ± 5.16 years) compared to the transferred group (7.59 ± 5.04 years), with a t-value of 0.67 and a p-value of 0.51, and a 95% confidence interval of the difference ranging from -1.09 to 2.21. Similarly, the mean weight was 32.21 ± 19.7 kg for the deceased group and 29.62 ± 18.06 kg for the transferred group, yielding a t-value of 0.847, a p-value of 0.398, and a 95% confidence interval of the difference from -3.44 to 8.61.

Table 3 shows the result of categorical prognostic factors and therapy outcomes in ICU using Pearson Chi-Square analysis that revealed several significant associations between patient characteristics and therapy outcomes in the ICU. Gender showed a statistically significant difference, with males having a higher transfer rate to specialized oncology departments (*P*=0.004). Patients with reduced BMI (*P*=0.009), concomitant diseases (*P*=0.007), and those in the high-risk group (*P*=0.037) were more likely to succumb in the ICU. Relapse of the disease was another significant factor (*P*=0.011), with patients experiencing one relapse showing higher mortality rates. Blood type, Rhesus factor, and heredity showed some trends but did not reach statistical significance for ICU outcomes.

The logistic regression analysis identified gender, concomitant diseases, and at-risk group classification as significant prognostic factors influencing ICU therapy outcomes in oncology patients. Males were three times more likely than females to experience a poorer outcome (Exp(B)=3.031, *P*=0.003). Patients with concomitant diseases were also significantly more likely to have adverse outcomes, with an odds ratio of 2.538 (Exp(B)=2.538, *P*=0.033). Conversely, being in a higher-risk group decreased the likelihood of adverse outcomes by 38% (Exp(B)=0.620, *P*=0.041). BMI, relapse of disease

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Table 3. Prognostic Factors (Patient Characteristics) and ICU Therapy Outcomes

Variable		Outcome of therapy in the ICU		Pearson Chi-Square	*P*-value
		Died	Transferred to the specialized oncology department		
Gender	Male	17 (17.5%)	80 (82.5%)	8.444	.004
	Female	33 (36.3%)	58 (63.7%)		
BMI	Reduced	26 (37.7%)	43 (62.3%)	6.862	.009
	promoted	24 (20.2%)	95 (79.8%)		
ALL Variant	Pro-B	12 (33.3%)	24 (66.7%)	5.817	.213
	Pre-B	6 (24.0%)	19 (76.0%)		
	Common	21 (27.6%)	55 (72.4%)		
	T cortical	5 (13.9%)	31 (86.1%)		
	*Other	6 (42.9%)	8 (57.1%)		
FAB Classification	L1	19 (31.7%)	41 (68.3%)	1.161	.281
	Other (L2 and L3)	31 (24.2%)	92 (75.8%)		
Concomitant diseases	No	35 (22.6%)	120 (77.4%)	7.292	.007
	**Yes	15 (45.5%)	18 (54.5%)		
At-risk group	Standard	7 (13.5%)	45 (86.5%)	6.613	.037
	Medium	9 (28.1%)	23 (71.9%)		
	High	34 (32.7%)	70 (67.3%)		
Relapse of the disease	No	26 (20.6%)	100 (79.4%)	9.109	.011
	1 time	19 (44.2%)	24 (55.8%)		
	2 times	5 (26.3%)	14 (73.7%)		
Blood Type	O(I)	21 (36.2%)	37 (63.8%)	7.328	.062
	A(II)	18 (25.0%)	54 (75.0%)		
	B(III)	5 (12.5%)	35 (87.5%)		
	AB(IV)	6 (33.3%)	12 (66.7%)		
Heredity Factor	No	47 (25.5%)	137(74.5%)	@Odds Ratio, [95% confidence interval] .114 [.012-1.126]	
	Yes	3 (75%)	1 (25%)		
Rhesus factor	Negative	2 (66.7%)	1 (33.3%)	@Odds Ratio, [95% confidence interval] 5.078 [.506, 64.379]	
	Positive	48 (25.9%)	137 (74.1%)		

* (T noncortical, In mature cell, biphenotypic (B+M)), ** Yes (Intrauterine infection + HCV, Itsenko-Cushing syndrome, Down's, DM, GERD, Mallory Weiss syndrome), @.2 cells (50.0%) have expected count less than 5. The minimum expected count is 80. That's why Odds Ratio with95% confidence interval calculated

showed no statistically significant influence on outcomes, although BMI (Exp(B)=1.845, *P*=0.093) displayed trends that warrant further investigation. The model's constant was not statistically significant (*P*=0.206), suggesting the importance of the included predictors in explaining ICU therapy outcomes as shown in Table 4.

Table 5 shows that a t-test analysis was conducted to examine the association between prognostic factors and the frequency of re-hospitalization during the same admission. Age showed no significant difference between patients re-hospitalized once (7.73 ± 5 years) and those re-hospitalized two or more times (7.79 ± 5.59 years), with a t-value of -0.049 and a p-value of 0.961. However, weight was significantly higher in patients re-hospitalized two or more times (48.98 ± 23.34 kg) compared to those re-hospitalized once (27.71 ± 16.16 kg), with a t-value of -5.568, *P*<0.001, and a 95% confidence interval of the difference ranging from -28.81 to -13.73.

Table 6 presents the Pearson Chi-square analysis examining the association between categorical prognostic factors and the frequency of re-hospitalization during the same ICU admission. Gender did not show a significant association with re-hospitalization frequency (*P*=0.699). Similarly, BMI category, ALL variant, FAB classification, presence of concomitant diseases, risk group classification, disease relapse, blood type, heredity factor, and Rhesus factor were not significantly associated with re-hospitalization frequency (all *P*>0.05). No categorical variable demonstrated a statistically significant influence on repeated re-hospitalization during the same ICU admission. Table 7 compares age and weight between patients with single and repeated ICU admissions using an independent samples t-test. No statistically significant differences were observed between the two groups for age (*P*=0.597) or weight (*P*=0.486). Patients with repeated ICU admissions had a mean age of 8.14 ± 5.44 years compared with 7.64 ± 4.98 years in those with a single ICU admission, while mean weights were 28.37 ± 16.86 kg and 30.77 ± 18.88 kg, respectively.

The 95% confidence intervals for both age and weight differences included zero, confirming the absence of significant differences between admission groups. Table 8 a chi-square analysis was performed to assess the association between ICU admission history (single vs. repeated) and various categorical variables. Gender showed no significant association with ICU admission history (*P*=0.831). BMI and ALL variant classifications also did not demonstrate a significant relationship with ICU admission history (*P*=0.409 and *P*=0.929, respectively). Concomitant diseases showed a non-significant trend (*P*=0.191), with patients having chronic conditions appearing more likely to have repeated ICU admissions. Relapse of the disease was significantly associated with ICU admission history (*P*=0.001); patients with one or more relapses were more likely to experience repeated ICU admissions compared to those without relapse. Other factors, such as FAB classification, at-risk group, blood type and heredity or Rhesus factor, did not show signifi-

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Table 4. Logistic Regression Analysis of Significant Prognostic Factors Influencing ICU Outcomes

Variable	B	S.E.	Wald	df	*P* value	Exp(B)	Reference Category
Gender	1.109	.378	8.624	1	.003	3.031	Female
BMI	.613	.364	2.827	1	.093	1.845	Reduced
Concomitant diseases	.931	.436	4.570	1	.033	2.538	No
At-risk group	-.478	.234	4.170	1	.041	.620	Standard
Relapse of the disease	-.280	.278	1.018	1	.313	.756	No relapse
Constant	-1.676	1.326	1.598	1	.206	.187	-

Table 5. Prognostic Factors Associated with Re-Hospitalization Frequency During the Same Admission

Variable	Re-hospitalization for Same Admission		t-value (*P*-value)	95% Confidence Interval of the Difference
	1 time (n=165) Mean ± SD	2 and more times (n=23) Mean ± SD		
Age	7.73 ± 5	7.79 ± 5.59	-.049 (.961)	(-2.29, 2.18)
Weight, kg	27.71 ± 16.16	48.98 ± 23.34	-5.568 (.000)	(-28.81, -13.73)

Table 6. Associations Between Categorical Prognostic Factors and Re-Hospitalization Frequency During the Same Admission

Variable		Re-hospitalization for Same Admission		Pearson Chi-Square	*P*-value
		1 time	2 and more times		
Gender	Male	86 (88.7%)	11 (11.3%)	.149	.699
	Female	79 (86.8%)	12 (13.2%)		
BMI	Reduced	60 (87.0%)	9 (13.0%)	.067	.796
	promoted	105 (88.2%)	14 (11.8%)		
ALL Variant	Pro-B	31 (86.1%	5 (13.9%)	4.428	.351
	Pre-B	22 (88.0%)	3 (12.0%)		
	Common	70 (92.1%)	6 (7.9%)		
	T cortical	31 (86.1%)	5 (13.9%)		
	*Other	11 (73.3%)	4 (26.7%)		
FAB Classification	L1	52 (86.7%)	8 (13.3%)	.099	.753
	Other (L2 and L3)	113 (88.3%)	15 (11.7%)		
Concomitant diseases	No	136 (87.7%)	19 (12.3%)	.000	.983
	**Yes	29 (87.9%)	4 (12.1%)		
At-risk group	Standard	46 (88.5%)	6 (11.5%)	1.555	.460
	Medium	26 (81.3%)	6 (18.8%)		
	High	93 (89.4%)	11 (10.6%)		
Relapse of the disease	No	112 (88.9%)	14 (11.1%)	1.539	.463
	1 time	38 (88.4%)	5 (11.6%)		
	2 times	15 (78.9%)	4 (21.1%)		
Blood Type	O(I)	50 (86.2%)	8 (13.8%)	2.335	.506
	A(II)	65 (90.3%)	7 (9.7%)		
	B(III)	33 (82.5%)	7 (17.5%)		
	AB(IV)	17 (94.4%)	1 (5.6%)		
Heredity Factor	No	162 (88.0%)	22 (12.0%)		
	Yes	3 (75.0%)	1 (25.0%)	@Odds Ratio, [95% confidence interval] 2.45 [.244,24.64]	
Rhesus factor	Negative	3 (100.0%)	0 (0.0%)	@Odds Ratio, [95% confidence interval]	
	Positive	162 (87.6%)	23 (12.4%)	1.14 [1.08, 1.20]	

* (T noncortical, In mature cell, biphenotypic (B+M)), ** Yes (Intrauterine infection + HCV, Itsenko-Cushing syndrome, Down's, DM, GERD, Mallory Weiss syndrome), @.2 cells (50.0%) have expected countless than 5. The minimum expected count is 80. That's why Odds Ratio with 95% confidence interval calculated

Table 7. Comparison of Age and Weight by ICU Admission History

Variable	ICU Admission History		t-value (*P*-value)	95% Confidence Interval of the Difference
	Single (n= 152) Mean ± SD	Repeated (n= 36) Mean ± SD		
Age	7.64 ± 4.98	8.14 ± 5.44	-.530 (.597)	(-2.35, 1.36)
Weight, kg	30.77 ± 18.88	28.37 ± 16.86	.698 (.486)	(-4.38, 9.17)

cant associations with ICU admission history. Odds ratio calculations for heredity and Rhesus factor were limited due to small sample sizes, but no significant trends were observed. This analysis highlights that disease relapse is a critical factor in predicting repeated ICU admissions.

Discussion

The current study shows that the majority of participants were aged 8-18 years (52.1%) and male (51.6%). Most participants had a weight ≤30 kg (56.9%) and reduced BMI (63.3%). High-risk patients made up 55.3%. This aligns with current findings regarding high-risk patients and that children with T-cell ALL or CNS leukemia had a higher likelihood of ICU admission, echoing the need for intensive monitoring in this demographic (11). Distinguishing features of the majority of cases are the lack of a history of a familial disease and the gene diversity that is often associated with mutations in PAX5, IKZF1, ETV6, and PTPN11 among others (12). Multidimensional data

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Table 8. Analysis of ICU Admission History by Categorical Variables

Variable		ICU Admission History		Pearson Chi-Square	*P*-value
		Single	Repeated		
Gender	Male	79 (81.4%)	18 (18.6%)	.045	.831
	Female	73 (80.2%)	18 (19.8%)		
BMI	Reduced	53 (76.8%)	11 (15.9%)	1.787	.409
	promoted	99 (83.2%)	16 (13.4%)		
ALL Variant	Pro-B	30 (83.3%)	6 (16.7%)	.870	.929
	Pre-B	19 (76.0%)	6 (24.0%)		
	Common	61 (80.3%)	15 (19.7%)		
	T cortical	29 (80.6%)	7 (19.4%)		
	*Other	13 (86.7%)	2 (13.3%)		
FAB Classification	L1	52 (86.7%)	8 (13.3%)	1.925	.165
	Other (L2 and L3)	100 (78.1%)	28 (21.9%)		
Concomitant diseases	No	128 (82.6%)	27 (17.4%)	1.706	.191
	**Yes	24 (72.7%)	9 (27.3%)		
At-risk group	Standard	47 (90.4%)	5 (9.6%)	4.243	.120
	Medium	25 (78.1%)	7 (21.9%)		
	High	80 (76.9%)	24 (23.1%)		
Relapse of the disease	No	111 (88.1%)	15 (11.9%)	13.107	.001
	1 time	29 (67.4%)	14 (32.6%)		
	2 times	12 (63.2%)	7 (36.8%)		
Blood Type	O(I)	46 (79.3%)	12 (20.7%)	.504	.918
	A(II)	60 (83.3%)	12 (16.7%)		
	B(III)	32 (80.0%)	8 (20.0%)		
	AB(IV)	14 (77.8%)	4 (22.2%)		
Heredity Factor	No	148 (80.4%)	36 (19.6%)	@Odds Ratio, [95% confidence interval] .804 [.749, .864]	
	Yes	4 (100.0%)	0 (0.0%)		
Rhesus factor	Negative	3 (100.0%)	0 (0.0%)	@Odds Ratio, [95% confidence interval] 1.242 [1.157, 1.333]	
	Positive	162 (87.6%)	23 (12.4%)		

* (T noncortical, in mature cell, biphenotypic (B+M)), ** Yes (Intrauterine infection + HCV, Itsenko-Cushing syndrome, Down's, DM, GERD, Mallory Weiss syndrome), @.2 cells (50.0%) have expected count less than 5. The minimum expected count is 80. That's why Odds Ratio with95% confidence interval calculated.

analysis is also used to discover hereditary germline variations that are connected to ALL risk (13). This emphasizes a close link between genetics and environmental factors that will lead to cautious personalized screening approaches, diagnosing, treating, and preventing children's ALL. Furthermore, the broader implications from these studies suggest that while hospitalization rates are high among children with ALL, especially those classified as high-risk, there is also a noteworthy need for improved preventive measures and supportive care strategies to mitigate risks associated with ICU admissions (14).

The current study shows that 26.6% of patients admitted to the ICU died, while 73.4% were transferred to oncology departments. Most patients had a single ICU admission during the study period (87.8%). This aligns with findings from another study indicating that 30% of children with acute leukemia required admission to a pediatric intensive care unit (PICU), often due to severe infections and other complications (15, 16). The next study emphasizes equal differences among genders, showing females have a slightly lower death rate than males. This phenomenon may be due to changes in the body triggered by treatments or due to certain sociocultural factors, such as different healthcare-seeking patterns. Despite females having lower mortality rates, they also experience higher standardized mortality ratios (SMR), suggesting challenges in treatment outcomes (17).

The current study revealed that there are no significant differences in age or weight between patients who died and those transferred to oncology departments (P > 0.05). However, gender, BMI, concomitant diseases, high-risk group classification, and relapse significant associations with ICU outcomes, with males having a higher transfer rate (*P*=0.004) and concomitant diseases being linked to higher mortality (*P*=0.007). Logistic regression analysis revealed that gender, concomitant diseases, and high-risk group classification were significant prognostic factors for ICU outcomes, with males being three times more likely to experience poorer outcomes (*P*=0.003) and patients with concomitant diseases having a higher likelihood of adverse outcomes (*P*=0.033). A study of unplanned cancer ICU admissions identified chronic conditions alongside mechanical ventilation and renal replacement as key mortality drivers (18). While no gender disparities noted in the current study are consistent with previous findings indicating that male patients often have poorer outcomes compared to females. This is particularly relevant given that males constituted a majority (52.2%) in the Indonesian study, which also highlighted the influence of demographic factors on treatment outcomes (19). Relapse remains a critical concern in ALL treatment. Another study found that most relapses occurred within the first 18 months post-diagnosis, aligning with findings from other studies indicating that early relapses are a significant predictor of poor outcomes (20).

The findings from the current study on re-hospitalization patterns among patients with Acute Lymphoblastic Leukemia (ALL) reveal significant insights into factors influencing hospital stays. Specifically, weight was notably higher in patients who were re-hospitalized two or more times (*P*<0.001), while age did not show a significant correlation (*P*=0.961). Similarly, a 2025 multi-

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center trial in pediatric ALL during maintenance therapy showed nutritional screening reduced readmission events (HR 0.397, from 46.5% to 28.6%) via improved albumin and immunity, with overweight z-scores (>2) noted as elevating infection-driven rehospitalizations in low-resource cohorts (21, 22). This aligns with the current study's findings, as both emphasize the importance of monitoring hospitalization frequency and its predictors. While research on children with ALL reported high infection rates during intensive treatment phases (average 4.5 episodes per patient), predominantly respiratory (48.1%) amid neutropenia, contributing to hospitalization burdens including one ICU admission (23). This suggests infection control is crucial for reducing rehospitalization rates, particularly for high-risk pediatric ALL patients. Similarly, prognosis depends on cytogenetic risk group, ethnicity, initial WBC count, and treatment intensity, all influencing hospitalization burden (24). Additionally, genetic and molecular studies, including metagenomics, highlight the complexity of the disease and challenges in identifying and managing early T-cell precursor (ETP) ALL (25). The role of comorbid conditions such as obesity and hypertension in the recovery and wellness of children with ALL is critically important and cannot be overstated (26).

Furthermore, the study identifies weight and BMI as critical factors influencing mortality rates. Individuals weighing less than 30 kg or with reduced BMI face higher mortality, underlining the necessity for early detection and ongoing monitoring of these risk factors to improve patient outcomes in pediatric ALL (27). Current findings align with prior pediatric ALL ICU research emphasizing clinical over genetic risk factors. Male sex and standard-risk classification protected against ICU mortality, driven by organ dysfunction rather than surveillance timing (28). Neutropenic sepsis and bleeding dominated mortality causes during ALL induction, mirroring our comorbidity-driven outcomes (29). Long-term diseases like intrauterine infection, HCV, Down's syndrome, and diabetes mellitus, too, prove to be other major impediments to predicting outcomes (30). Therefore, these results confirm the importance of early screening and monitoring of precursor conditions and certain patient features as precursors in determining.

Blood type showed non-significant ICU outcome trends in our cohort. Research confirms ABO blood groups influence disease susceptibility, with blood group A linked to higher cancer risk (including gastric, ovarian, and colon cancers) compared to type O, though molecular mechanisms require further study (31), earlier age groups and familial risks, as well as genetic ancestry and molecular subtypes (32). The majority of ICU admissions occurred early in treatment, especially among children with T-cell ALL or CNS leukemia, indicating a higher risk for these groups (11). Another pediatric AML study reported high early mortality 4.9% and treatment-related deaths 3.4% (33). Furthermore, research has shown that despite high admission rates to ICUs, effective treatment protocols have led to improved outcomes for children with ALL. Conventional chemotherapy combined with supportive care has resulted in high remission rates, although disparities exist between high-income and low-income countries due to access to advanced treatments (34). While the treatment regimen for ALL typically includes induction, consolidation, and maintenance phases, each requiring varying degrees of hospitalization due to potential complications such as infections or treatment-related toxicities (35). The intensity of these phases often correlates with the necessity for ICU care.

Study Limitations

There are a number of limitations to this study. Since it was carried out in only one tertiary pediatric care center (SCPC), it is difficult to extrapolate the findings to other healthcare contexts. The design is retrospective, and the analysis of subgroups was limited; some subgroups, in particular the Heredity and Concomitant Diseases subgroups, were quite small, which may adversely affect statistical power and introduce bias. Beyond this, the lack of data regarding long-term follow-up, and certain untracked variables, constrain the analysis. To confirm these findings and more fully explain the relationships identified, further studies with multiple centers, larger sample sizes, and longer follow-up periods are needed.

Conclusion

In conclusion, this retrospective cohort study examined the characteristics, outcomes, and prognostic factors of children with ALL admitted to the ICU. The results provide valuable insights into the demographic profile, disease-related variables, and therapeutic outcomes for this patient group.

Demographically, the majority of participants were male and aged 8-18 years. The most common ALL variant was the common subtype, and a predominant number of patients were classified in the high-risk group. These findings suggest that ALL in this cohort is largely observed in adolescents, with high-risk disease variants being the most prevalent. This aligns with global trends where risk factors and patient age influence the severity of the disease and the intensity of the treatment regimen.

Regarding ICU outcomes, 26.6% of the patients succumbed during their ICU stay, while the remaining 73.4% were successfully transferred to specialized oncology departments for continued care.

Statistical analyses revealed several prognostic factors associated with ICU outcomes. Gender was found to significantly influence outcomes, with males exhibiting higher transfer rates to oncology departments. Additionally, concomitant diseases (comorbid conditions), reduced BMI, and being in the high-risk group were significant predictors of mortality in the ICU. The relapse of disease was also a significant factor, with patients experiencing one relapse showing higher mortality rates. These factors highlight the importance of considering comorbid conditions, disease relapse, and risk group classification when predicting patient outcomes in critically ill children with ALL.

Logistic regression analysis further supported these findings, revealing that male gender and the presence of concomitant diseases (comorbid conditions) were signifi-

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cant predictors of adverse ICU outcomes. Interestingly, being in a higher-risk group was associated with a reduced likelihood of poor outcomes, suggesting that while high-risk patients receive intensive care, they may benefit more from specialized oncology treatments after ICU stabilization.

Finally, the study identified weight as a key factor associated with re-hospitalization frequency. Patients who were re-hospitalized two or more times had significantly higher mean weights compared to those re-hospitalized once. This may suggest that children with higher body mass are more likely to experience complications, requiring repeated ICU admissions.

In conclusion, this study provides critical insights into the prognostic factors influencing ICU outcomes in children with ALL. The findings emphasize the importance of gender, concomitant diseases, relapse, BMI, and risk group classification in determining therapy outcomes. These factors should be considered when managing pediatric ALL patients in the ICU to optimize treatment strategies and improve patient outcomes. Further studies are warranted to explore these associations in more depth and to develop targeted interventions for high-risk groups.

Authors' Contributions

Yedil Kurakbayev (YK): Conceptualization; Methodology; Supervision; Writing-original draft; Project administration.

Kuanysh Umbetov (KU): Investigation (data collection); Data curation; Validation; Visualization; Writing-review & editing.

Yergali Sarsekbayev (YS): Formal analysis; Statistical analysis; Software; Validation; Writing-review & editing.

Botagoz Turdaliyeva (BT): Resources; Clinical oversight; Methodology (clinical aspects); Critical revision of the manuscript; Writing—review & editing.

Lyazat Manzhuova (LM): Ethics coordination; Project administration; Supervision; Interpretation of results; Writing-review & editing.

All authors substantially contributed to the study's design and interpretation, and all authors read and approved the final manuscript.

Ethical Considerations

Used anonymized data for analysis to protect patient privacy.

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Conflict of Interests

The authors declare that they have no competing interests.

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