Original Article

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Clinical Outcomes of Acute Leukemia in Children Less Than 2 Years: Experience from a Tertiary Center in Thailand

Umaporn Yam-ubon, M.D.[1], Natsaruth Songthawee, M.D.[1], Shevachut Chavananon, M.D.[1], Pornpun Sripornsawan, M.D.[1], Sirinthip Kittivisuit, M.D.[1], Edward B McNeil, M.Sc.[2], Thirachit Chotsampancharoen, M.D.[1]

[1]Division of Hematology and Oncology, Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

[2]Department of Epidemiology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

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Abstract:

Objective: This study aimed to examine the prognostic factors and treatment outcomes of patients with acute leukemia aged under 2 years.

Material and methods: The medical records of acute leukemia patients aged under 2 between January 1979 and December 2021 were retrospectively reviewed. The Kaplan-Meier method was used to calculate the event-free survival (EFS) and overall survival (OS) rates. A univariate Cox proportional hazards regression model was used to identify clinical factors associated with poor EFS and OS. A p-value<0.05 was considered statistically significant.

Results: Over the 43-year study period, 137 children with acute leukemia aged under 2 years of age were identified. Of these, 70 (51.1%) had acute lymphoblastic leukemia (ALL) and 67 (48.9%) had acute myeloid leukemia (AML). After induction, 89.1% of ALL patients achieved complete remission, with an induction death rate of 3.2%. The 5-year OS and EFS rates were 46.0% and 41.0%, respectively. After induction, 44.8% of the AML patients achieved complete remission, with an induction death rate of 29.3%. The 5-year OS and EFS rates in this group were 10.0% and 9.0%, respectively. No significant prognostic factors were identified to predict survival outcomes in children with AML under 2 years.

Conclusion: Both ALL and AML childhood leukemia patients aged under 2 years had poor survival outcomes.

Keywords: acute lymphoblastic leukemia, acute myeloid leukemia, infant leukemia, treatment outcomes

Contact: Thirachit Chotsampancharoen, M.D.
Division of Hematology and Oncology, Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
E-mail: cthirachit@yahoo.com

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Introduction

Infant leukemia has distinctive biology and clinical features. It has aggressive features, including hyperleukocytosis, hepatosplenomegaly, central nervous system (CNS) involvement, leukemic cutis, and cytogenetic abnormalities. These aggressive features and unfavorable cytogenetics lead to poor treatment outcomes in infant leukemia; especially in those with acute lymphoblastic leukemia (ALL)[1,2]. The definition of infant leukemia is acute leukemia in infants diagnosed in the first 12 months of life. The survival rate of infant ALL is worse than childhood ALL. Infant ALL has been reported as having EFS rates ranging from 31.9 to 47.0%[2-5] and OS rates ranging from 33.7 to 58.2%[4,5]. Infant acute myeloid leukemia (AML) also has lower EFS and OS rates than childhood AML, with reported EFS rates of 41.0% and 54.0% and OS rates of 54.0% and 70.4%[6,7]. The cause of low EFS and OS rates in this age group is likely due to treatment-related toxicities and immaturity of the lungs, liver, and brain[8-10]. As a result, the treatment outcomes of infant leukemia compared with older children are poorer. However, patients aged between 1 and 2 years also tend to have worse outcomes than older children, similar to infant leukemia patients[10]. Various studies have combined infants less than 12 months with those aged 1-2 years as having similar patient characteristics and survival outcomes[4,6,11-15]. However, there are few studies evaluating prognostic factors and treatment outcomes of children aged under 2 years with acute leukemia in developing countries[4,12]. Earlier studies have reported that the survival outcome of children with ALL aged 1-2 years was better than infants less than 1 year, but still worse than the older age groups[4,12]. Hence, further studies are required to determine the survival rates of very young children with acute leukemia. This study aimed to examine the prognostic factors and survival outcomes in children aged under 2 years diagnosed with acute leukemia in Southern Thailand.

Material and Methods

Patients

We retrospectively reviewed the medical records of children aged under 2 years who were newly diagnosed with acute leukemia; between January 1979 and December 2021, treated at Songklanagarind Hospital; the largest tertiary referral center in southern Thailand. The study was approved by the Institutional Ethics Committee.

The variables collected included gender, age at diagnosis, initial presentation, leukemia subtype, treatment, complete remission (CR), complications during the induction phase, relapse, site of relapse (if any), survival status at the time of last follow-up; and cause of death (if deceased). Patients with incomplete data or therapy discontinuation were excluded.

Diagnosis of acute leukemia

The initial diagnosis of acute leukemia was made by morphologic assessment, immunophenotype by flow cytometry, and immunochemical examinations of bone marrow material obtained through aspiration and/or biopsy. The criterion of >20% lymphoblasts or myoblasts was used for definitive diagnosis. In cases of AML, even if the blast threshold of 20% was not met, a diagnosis of AML was made when evidence of recurrent genetic abnormalities, such as t (8;21), inv (16), or t (16;16) was found[8]. Changes in the subtype classifications of acute leukemia for ALL and AML occurred during the study period. Before 2000, the ALL subtype was based on the French-American-British (FAB) classification, for which patients were divided into three subtypes: ALL-L1, -L2, and -L3 (Burkitt leukemia) categories. The reason for using the FAB classification during that period was that a cluster of differentiation markers had not yet been introduced into our center. As of the year 2000, patients diagnosed with ALL have been divided into three subtypes: B-cell, T-cell, and Burkitt-cell

leukemia; based on the World Health Organization ALL classification system. We excluded patients with Burkitt leukemia, and the AML subtypes were based on the FAB classification, which categorizes AML as the M0–M7 subtype. CNS involvement was defined as white blood cells ≥5/μL with evident blasts present in the cytospin of cerebral spinal fluid (CSF), cranial nerve palsies, or intracerebral disease on imaging.

Treatment of ALL

The patients enrolled in the study were divided into four groups based on the different protocols used to treat ALL during the study period, designated as study periods 1–4. During study period 1 (1979–1986), patients received the Siriraj II Protocol[15]. During study period 2 (1987–2005), the Children's Cancer Group (CCG)–105 and CCG–106 classifications were used for intermediate and poor-risk patients, respectively[16,17]. In study period 3 (2006–2013), ALL patients were treated using the Thai Pediatric Oncology Group (ThaiPOG) national protocol, which was based on the Pediatric Oncology Group (POG) and CCG. The ALL–01–05 protocol was used for standard-risk ALL patients, while the ALL–02–05 protocol was used for high-risk ALL patients[18,19]. In study period 4 (2014–2021), ALL patients were treated using the ThaiPOG protocol, which was based on the Children's Oncology Group (COG). The COG–AALL0631 regimen was used in infants aged less than 1 year. The modified COG–AALL0932 and AALL1131 regimens were used in children aged 1–2 years having standard and high/very high risks, respectively[20].

Treatment of AML

The AML patients were divided into the same 4 periods. During study period 1 (1979–1993), the AML–Berlin–Frankfurt–Münster (BFM)–78 regimen was used[21]. In study period 2 (1994–2007), the AML–BFM–83 regimen was used[22]. In study period 3 (2008–2013), AML patients were treated using the ThaiPOG protocol, which was based on AML–BFM–98 regimen[23]. In period 4 (2014–2021), AML patients were treated using the most recent version of the ThaiPOG protocol, which was modified from the COG–AAML 1031 regimen. Low-risk patients received the AML–1301 protocol, whereas high-risk patients received the AML–1302 protocol[24].

Outcomes and complications of treatment

CR was defined as a percentage of blast cells in the bone marrow <5% (M1 marrow) and no blast cells in the CSF at the end of the induction phase. During induction chemotherapy, complications were monitored, including bleeding, tumor lysis syndrome (TLS), disseminated intravascular coagulation (DIC), acute kidney injury (AKI), CNS complications, and intensive care unit (ICU) admission. Tumor lysis syndrome was diagnosed based on the Cairo–Bishop definition. A diagnosis of DIC was based on the diagnostic criteria of the International Society on Thrombosis and Hemostasis (ISTH). Acute kidney injury was defined according to the Kidney Disease: Improving Global Outcomes criteria. CNS complications included seizure, stroke, and intracranial bleeding.

A relapse was diagnosed at any return of symptoms after initially achieving CR. Isolated bone marrow relapse was defined as >20% lymphoblasts or myeloblasts in the bone marrow. Isolated CNS relapse was defined as ≥5/μL leukocytes, with identifiable blast cells in a cytocentrifuged preparation of CSF, the development of cranial nerve palsies or intracranial disease, or abnormal intracranial imaging. Isolated testicular relapse was defined as the presence of unilateral or bilateral testicular enlargement, with biopsy-proven leukemic involvement in the absence of bone marrow involvement (<5% blast cells). The presence of ≥5% blast cells in the bone marrow and extramedullary disease was categorized as a combined relapse.

Cancer-related death was defined as death due to the burden or progression of disease; therefore, we refer to death occurring within 7 days of starting induction chemotherapy, death due to refractory disease, or subsequent relapse. Treatment-related mortality was defined as death in the absence of progressive disease, which included death from infection, bleeding, or organ dysfunction, occurring 7 days or more after starting induction chemotherapy[25].

Statistical analysis

For continuous variables, descriptive statistics are presented using mean and standard deviation or median and interquartile range (IQR): as appropriate. For categorical variables, descriptive statistics are presented using frequency with percentage. EFS was defined as the time from diagnosis to first failure (failure to achieve CR, death, or relapse). OS was defined as the period from diagnosis to death. The Kaplan-Meier method was used to calculate the EFS and OS rates. A univariate Cox proportional hazards regression model was used to identify risk factors associated with poor survival outcomes. A multivariate Cox regression model was used to predict EFS and OS, based on statistically significant factors from the univariate analysis. Confidence intervals (CI) were computed with a 95% confidence level. A p-value of 0.05 or less was considered statistically significant.

Results

During the 43-year study period, 137 (12.8%) were aged less than 2 years, of which 70 (51.1%) had ALL and 67 (48.9%) had AML. Forty-eight patients were aged less than 1 year, of which 20 (41.7%) had ALL and 28 (58.3%) had AML.

The ALL group

Of the 70 ALL patients aged less than 2 years, the median age at diagnosis was 16 months (IQR 10.8-21); whilst 20 (28.6%) were aged less than 1 year. The common presenting features were: hepatomegaly (92.8%), pallor (87.1%), fever (85.7%), splenomegaly (80.0%), lymphadenopathy (58.6%) and clinical bleeding (42.8%). The median white blood cells (WBC) and peripheral blast counts were 33.6×109/L (IQR 12.3-107.4) and 66.0% (IQR 24.0-89.2), respectively. There were 18 (25.7%) ALL patients with hyperleukocytosis. Of the 42 ALL patients that had CSF cytology, 5 (11.9%) patients had CNS involvement. There were 36 (51.4%) patients with B-ALL and 4 (5.7%) patients with T-ALL, while the remaining 30 (42.9%) patients were categorized using the FAB classification. The patient characteristics, treatment outcomes, and complications during induction therapy are presented in Table 1.

Among 64 patients having received induction therapy and assessed after complete treatment, 57 (89.1%) achieved remission after induction, and only two (3.2%) died during the induction phase. The most common complications during induction chemotherapy were TLS (27.1%), bleeding (18.6%), and DIC (15.7%), with 8.7% requiring ICU admission. The relapse rate was 40%. Isolated bone marrow (46.4%) was the most common site of relapse, followed by isolated CNS (28.6%) and combined sites (25.0%).

The 5-year OS and EFS rates of the ALL patients were 46.0% and 41.0%, respectively. As shown in Figure 1, the 5-year OS of patients aged less than 1 year was significantly lower than in those aged 1-2 years (21.0% vs. 55.0%, p-value=0.0019). As shown in Figure 2, the 5-year EFS of patients aged less than 1 year was significantly lower than in those aged 1-2 years (19.0% vs 52.0%, p-value <0.001). The 5-year OS of patients with B-ALL was lower than those with T-ALL (40.0% vs. 100.0%, p-value=0.2). The survival rates between males and females were not significantly different. The most common cause of death among the 41 ALL cases having died was cancer-related (80.5%), followed by infection (14.6%) and bleeding (2.4%). The OS rates of patients with ALL, based on clinical characteristics, are shown in Table 2.

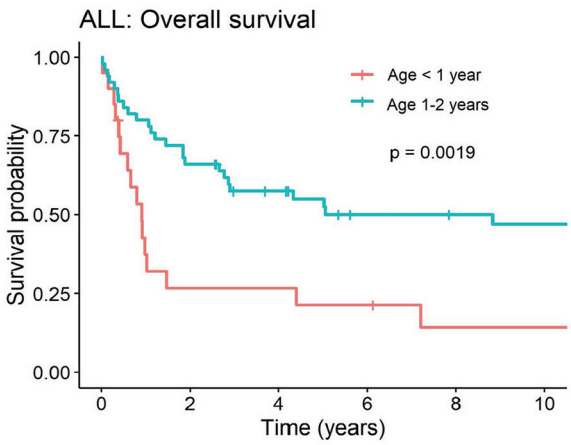
Table 1 Patient characteristics and treatment outcomes of infants with ALL and AML

Characteristic	ALL, n (%) n=70	AML, n (%) n=67	p-value
Median age (months)	16 (10.8-21.0)	15 (8.0-20.0)	0.18
Sex			0.91
Male	38 (54.3)	38 (56.7)	
Female	32 (45.7)	29 (43.3)	
WBC (x10^3/μL), median (IQR)	33.6 (12.3-107.4)	41.2 (14.4-108.7)	0.71
Peripheral blast (%), median (IQR)	66 (24.0-89.2)	25 (7.0-67.0)	0.001
Hemoglobin (g/dL), median (IQR)	6.9 (5.5-8.5)	7.1 (5.9-8.4)	0.50
Platelet (x10^3/μL), median (IQR)	27.0 (13.0-93.5)	26.0 (12.0-61.0)	0.46
CNS involvement[a]	5/42 (7.1)	5/31 (7.5)	0.99
Down syndrome	-	11 (16.4)	
Treatment outcomes			
Remission of induction			<0.001
Yes	57 (89.1)	26 (44.8)	
Died during induction	2 (3.2)	17 (29.3)	
Relapse	28 (40.0)	28 (41.8)	0.16
Relapse site			0.005
BM	13 (46.4)	24 (85.7)	
CNS	8 (28.6)	1 (3.6)	
Combined	7 (25.0)	3 (10.7)	
Death	41 (58.6)	60 (89.5)	<0.001
Cause of death			0.29
Cancer-related	33 (80.5)	38 (63.3)	
Infection	6 (14.6)	15 (25.0)	
Bleeding	1 (2.4)	4 (6.7)	
Complications during induction			
TLS	19 (27.1)	13 (19.4)	0.42
DIC	11 (15.7)	22 (32.8)	0.03
Bleeding	13 (18.6)	35 (49.3)	<0.001
CNS complications[b]	2 (2.9)	11 (16.4)	0.014
Acute kidney injury	4 (5.7)	5 (7.5)	0.74
ICU admission	6 (8.6)	29 (43.3)	<0.001

[a]Patient with data [b]CNS complications include seizure, stroke, intracranial bleeding ALL=acute lymphoblastic leukemia, AML=acute myeloid leukemia, CNS=central nervous system, DIC=disseminated intravascular coagulation, ICU=intensive care unit, IQR=interquartile range, TLS=tumor lysis syndrome, WBC=white blood cells

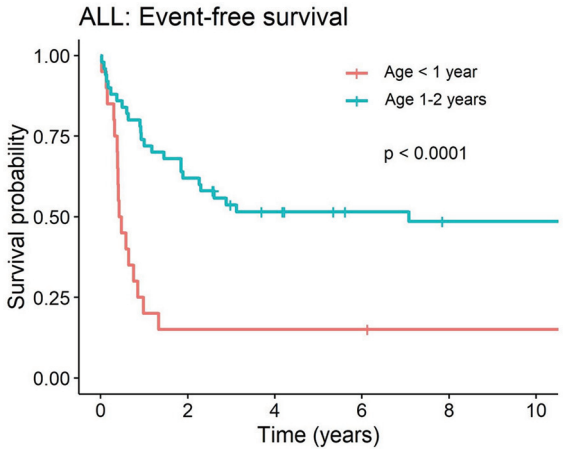
Age and WBC count were the two prognostic factors associated with OS. Patients aged 1-2 years had a hazard ratio of 0.38 compared to patients aged less than 1 year (p-value=0.003). Patients with a WBC count ≥50×109/L had a hazard ratio of 3.24 compared to patients with a WBC count <10×109/L (p-value=0.031). There were no differences in OS between the two genders nor four study periods. Table 3 shows the univariate analysis of risk factors for OS, based on the clinical data of children with acute leukemia.

WBC count was the only risk factor associated with OS. When compared to patients with a WBC count <10×10^9/L, patients with a WBC count ≥50×10^9/L had a hazard ratio of 3.51 (p-value=0.03). Age, gender, and study period were not significantly associated with OS. Table 4 shows the multivariate analysis of risk factors for OS, based on the clinical data of children with acute leukemia.



ALL=acute lymphoblastic leukemia

Fgure 1 Overall survival of patients with acute lymphoblastic leukemia



ALL=acute lymphoblastic leukemia

Fgure 2 Event free survival of patients with acute lymphoblastic leukemia

Table 2 Overall survival of patients with ALL and AML, based on clinical characteristics

Characteristic	ALL (N=70)			AML (N=67)		
	No. of patients, n (%)	5-year OS, % (95% CI)	p-value	No. of patients, n (%)	5-year OS, % (95% CI)	p-value
Sex			0.7			0.9
Male	38 (54)	48 (34, 68)		38 (57)	7.9 (2.7, 23)	
Female	32 (46)	42 (28, 64)		29 (43)	14 (5.6, 34)	
Age (years)			0.002			0.5
<1	20 (29)	21 (9.0, 51)		28 (42)	7.1 (1.9, 27)	
1-2	50 (71)	55 (43, 71)		39 (58)	13 (5.7, 29)	
WBC (/μL)			0.04			0.5
<10,000	12 (17)	67 (45, 99)		11 (16)	18 (5.2, 64)	
10,000-49,999	28 (40)	55 (39, 78)		26 (39)	12 (4.0, 33)	
≥50,000	30 (43)	30 (17, 52)		30 (45)	6.7 (1.7, 25)	
CNS involvement	5/42 (7.1)	40 (14, 100)	0.9	5/31 (7.5)	-	0.6
Period*			0.7			0.9
1	5 (7.1)	20 (3.5, 100)		6 (8.9)	-	
2	29 (41.4)	46 (31, 69)		25 (37.3)	16 (6.5, 39)	
3	27 (38.6)	48 (32, 71)		21 (31.3)	4.8 (0.7, 32)	
4	9 (12.9)	44 (18, 100)		15 (22.3)	13 (3.7, 48)	
Immunophenotype						
B-ALL	36 (51.4)	40 (26, 60)	0.2	-	-	
T-ALL	4 (5.7)	100 (100, 100)		-	-	
FAB	30 (42.9)	45 (30, 67)		-	-	
AML	-	-		67 (100)	10 (5.2, 21)	0.7

[a]Patient with data [b]For ALL, Period 1: 1979-1986; Period 2:1987-2005; Period 3: 2006-2013; Period 4: 2014-2021 For AML, Period 1: 1979-1993; Period 2:1994-2007; Period 3: 2008-2013; Period 4: 2014-2021 ALL=acute lymphoblastic leukemia, AML=acute myeloid leukemia, CNS=central nervous system, FAB=French-American-British, OS=overall survival, WBC=white blood cells

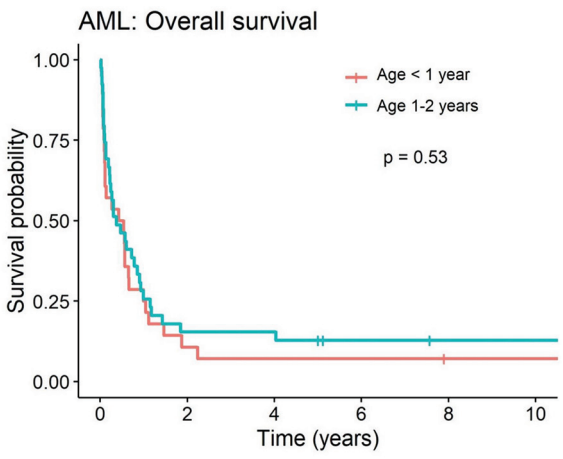
WBC count ≥50×10^9/L was also the only risk factor associated with worse OS (HR 3.51, p-value<0.03) when compared to patients with a WBC count <10×10^9/L.

AML group

Of the 67 AML patients aged less than 2 years of age, the median age at diagnosis was 15 months (IQR 8-20), while 28 (41.8%) were aged less than 1 year. The most common presenting features were hepatomegaly (97.0%), splenomegaly (91.0%), fever (89.6%), and pallor (89.6%). Approximately half had clinical bleeding (47.8%) and lymphadenopathy (44.8%). The median WBC and peripheral blast counts were 41.2×10^9/L (IQR 14.4-108.7) and 25.0% (IQR 7.0-67.0), respectively. There were 18 (26.9%) patients with hyperleukocytosis. Of the 31 patients having had CSF cytology; 5 (16.1%) had CNS involvement (Table 1). According to the FAB classification, 6.0%, 3.0%, 9.0%, 16.4%, 4.5%, and 37.3% had the AML-M1, M2, M4, M5, M6, or M7 subtypes, respectively, while the remaining 16 (23.8%) patients were not classified. There were no patients with the AML-M3 subtype identified in this study.

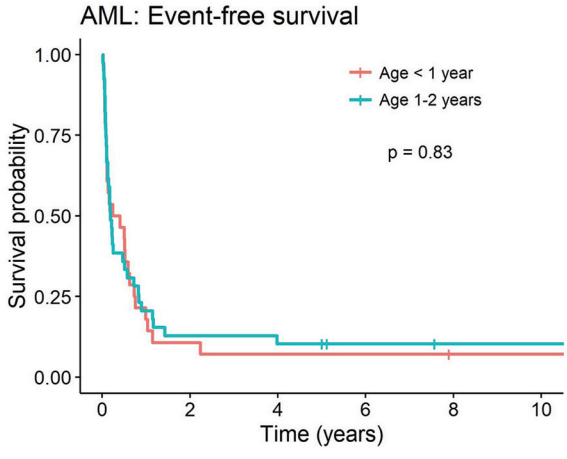
Among 58 patients having received induction therapy and assessed after complete treatment, 26 (44.8%) patients achieved remission after induction, and 17 (29.3%) died during the induction phase. The most common complications during induction chemotherapy were bleeding (49.3%), DIC (32.8%), TLS (19.4%), and CNS complications (16.4%), with 43.3% requiring ICU admission. The relapse rate was 41.8%. Isolated bone marrow (85.7%) was the most common site of relapse, followed by isolated CNS (3.6%) and combined relapse (10.7%). The patient characteristics, treatment outcomes, and complications during induction therapy are presented in Table 1.

The 5-year OS and EFS rates of AML patients aged less than 2 years were 10% and 9%, respectively. There were no significant differences in OS and EFS rates between genders, age groups, WBC count, or study periods. As shown in Figures 3 and 4, the 5-year OS and EFS rates of patients aged less than 1 year were not significantly different from those aged 1-2 years (7.1% vs. 13.0%, p-value=0.53 and 7.1% vs 12.0%, p-value=0.83, respectively). The most common cause of death was cancer-related (63.3%),



AML=acute myeloid leukemia

Figure 3 Overall survival of patiens with acute myeloid leukemia



AML=acute myeloid leukemia

Figure 4 Event free survival of patients with acute myeloid leukemia

Table 3 Univariate analysis of risk factors for overall survival by clinical parameters

Characteristic	ALL (N=70)			AML (N=67)		
	No. of patients, n (%)	5-year OS, % (95% CI)	p-value	No. of patients, n (%)	5-year OS, % (95% CI)	p-value
Sex			0.7			0.9
Male	38 (54.2)	48 (34, 68)		38 (57)	7.9 (2.7, 23)	
Female	32 (45.7)	42 (28, 64)		29 (43)	14 (5.6, 34)	
Age (year)			0.002			0.5
<1	20 (28.5)	21 (9.0, 51)		28 (42)	7.1 (1.9, 27)	
1-2	50 (71.4)	55 (43, 71)		39 (58)	13 (5.7, 29)	
WBC (/μL)			0.04			0.5
<10,000	12 (17.1)	67 (45, 99)		11 (16)	18 (5.2, 64)	
10,000-49,999	28 (40.0)	55 (39, 78)		26 (39)	12 (4.0, 33)	
≥50,000	30 (42.8)	30 (17, 52)		30 (45)	6.7 (1.7, 25)	
CNS involvement	5/42 (7.1)	40 (14, 100)	0.9	5/31 (7.5)	-	0.6
Period*			0.7			0.9
1	5 (7.1)	20 (3.5, 100)		6 (8.9)	-	
2	29 (41.4)	46 (31, 69)		25 (37.3)	16 (6.5, 39)	
3	27 (38.6)	48 (32, 71)		21 (31.3)	4.8 (0.7, 32)	
4	9 (12.9)	44 (18, 100)		15 (22.3)	13 (3.7, 48)	
Immunophenotype						
B-ALL	36 (51.4)	40 (26, 60)	0.2	-	-	
T-ALL	4 (5.7)	100 (100, 100)		-	-	
FAB	30 (42.9)	45 (30, 67)		-	-	
AML	-	-		67 (100)	10 (5.2, 21)	0.7

*For ALL, Period 1: 1979-1986; Period 2:1987-2005; Period 3: 2006-2013; Period 4: 2014-2021 For AML, Period 1: 1979-1993; Period 2:1994-2007; Period 3: 2008-2013; Period 4: 2014-2021 ALL=acute lymphoblastic leukemia, AML=te myeloid leukemia, HR=hazard ratio, CI=confidence interval, OS=overall survival, WBC=white blood cells

Table 4 Multivariate Cox regression model to determine risk factors of overall survival

Characteristic	ALL			AML		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (months), ref: <12						
12-24	0.53	0.26, 1.08	0.08	0.70	0.39, 1.26	0.24
Sex, ref: Male						
Female	1.04	0.54, 2.01	>0.90	0.95	0.52, 1.73	0.86
WBC (/μL), ref: <10,000						
10,000-49,999	2.62	0.78, 8.76	0.12	1.32	0.57, 3.05	0.52
≥50,000	3.51	1.10, 11.2	0.03	1.23	0.53, 2.87	0.64
Period*, ref: 1						
2	0.36	0.10, 1.26	0.11	1.14	0.41, 3.15	0.80
3	0.40	0.09, 1.86	0.20	0.76	0.28, 2.07	0.59
4	0.26	0.04, 1.51	0.13	0.66	0.23, 1.91	0.44

*For ALL, Period 1: 1979-1986; Period 2:1987-2005; Period 3: 2006-2013; Period 4: 2014-2021 For AML, Period 1: 1979-1993; Period 2:1994-2007; Period 3: 2008-2013; Period 4: 2014-2021 ALL=acute lymphoblastic leukemia, AML=acute myeloid leukemia, HR=hazard ratio, CI=confidence interval, OS=overall survival, WBC=white blood cells

followed by infection (25.0%) and bleeding (6.7%). The overall survival rates of patients with AML, based on clinical characteristics, are shown in Table 2. There were no risk factors associated with overall survival from the univariate and multivariate analyses, as shown in Tables 2 and 3.

Discussion

Our study examined the treatment outcomes and prognostic factors of children with acute leukemia aged under 2 years. The clinical features, namely: gender, WBC count, subtype, and CNS involvement, of the children with ALL, were similar to other studies. The median WBC count in our study was 33.6×10^9/L; similar to a study from China, with a count of 46.4×10^9/L[26]. The proportion of patients with a WBC count $\geq50\times10^9$/L was 43.0%, which was lower than in previous studies (range: 46.3–71.6%)[26]. The CNS involvement in our study was 11.9%, which was similar to previous studies (range: 12.9–24.8%)[3,12,27]. The B-cell precursor was the most common subtype (90.0%), again similar to other studies (range: 73.0–97.0%)[1,3,12,27].

The treatment outcomes of ALL in this study were inferior to other studies from developed countries. The CR rate in this study was 89.1%, which was similar to studies performed in Europe and America, in which the rates ranged from 89.0 to 94.0%[3,27,28]. Induction death of ALL patients was 3.2% in our study, (range: 3.7–7.8%)[3,27,28]; additionally, the relapse rate in our study was 40.0%, both being similar to previous studies[3,27,28]. BM relapse in our study was the most common site of relapse (46.4%), similar to the COG P9407 study[28]. In a subgroup analysis of infants aged less than 1 year, the 5-year OS rate was 21.0%, which was consistent with studies from upper-middle-income countries, including Brazil, China, and Turkey[12,26,29] although the rate was lower than in other studies from high-income countries, ranging from 43.0% to 85.0%[30–33]. Most earlier studies reported that treatment outcomes of children with T-cell ALL were poorer than for children with B-cell ALL. We found that the 5-year OS of patients with T-cell ALL was not different from patients with B-cell ALL, but our sample size of T-cell patients was too small to be statistically powerful. On univariate analysis, age <1 year was associated with inferior overall survival, which was similar to a study from India[7]. On both univariate and multivariate analysis, we found that a WBC count $\geq50\times10^9$/L was associated with inferior overall survival, again similar to other studies[4,28].

The clinical features of children with AML were also similar to other studies, including gender, WBC count, AML subtype, and CNS involvement[6,9,34]. The CNS involvement in our study was 16.1%, which was similar to previous studies (range: 14.0–18.3%)[9,34]. The complete remission rate in previous studies in developed countries ranged from 86.0–92.0%[6,9,34], while the rate in developing countries ranged from 43.0–72.0%. In our study, the rate was 44.8%[35,36]. Induction death in our study was higher than in other studies (29.3% vs 5.1–7.2%)[9,34]. The AML relapse rate was 41.8% in our study, which was higher than in other studies, which ranged between 31.0% and 37.0%[6,9,34,37]. Isolated bone marrow relapse was the most common site of relapse in our study (85.7%), similar to other studies[9,37]. In our study, the 5-year EFS rate of infant AML was 9.0%, which was lower than in other studies from developed countries, which ranged from 32.0 to 67.0%. Also, the 5-year OS rate was 10.0%, which was lower than the other studies' rates of 61.0–75.0%[6,34,37,38]. There were no significant predictive factors associated with treatment outcomes of children with AML in our study. No difference in survival outcomes was found between age groups, which was similar to previous studies[9].

The survival outcomes of leukemia from our study were lower than in studies from developed countries; especially in infant AML. A quarter of the children with AML having received chemotherapy died during induction.

This was the most common cause related to infectious complications leading to a higher prevalence of DIC compared to ALL patients, which was also found in a previous study[39]. To improve the treatment outcomes, strategies to prevent early treatment-related infection are required, including antimicrobial prophylaxis when indicated, supportive care, early detection, and appropriate antimicrobial therapy with a multidisciplinary team approach. According to the distinctive molecular lesions of infant leukemia, identifying individual risk factors and designing appropriate intensive therapy may improve survival outcomes. Infants have unique pharmacokinetic and pharmacodynamics profiles, so chemotherapy dose modification might reduce treatment toxicities and lead to better outcomes. In addition, hematopoietic stem cell transplant should be incorporated into the treatment to improve the outcomes.

Certain limitations of this study should be acknowledged. First, there is a potential information bias in retrospective studies. Second, our study covered a long period during which advances in diagnostic methods, chemotherapy regimens, and supportive care were made. Third, our study did not include molecular studies, which are important for identifying risk stratification and treatment of infant leukemia. Finally, there was a possibility of referral bias because our setting is a major tertiary healthcare facility and university hospital that treats predominantly high-risk and complicated cases of infant leukemia across Southern Thailand.

Conclusion

Childhood leukemia patients aged less than 2 years, both ALL and AML, had poor survival outcomes and high relapse rates when compared to developed countries. Future prospective studies with risk-adapted therapy are needed to improve survival outcomes among these patients.

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Conflict of interest

The authors report there are no competing interests to declare. There was no funding support for this study.

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