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The Survival of Childhood Acute Lymphoblastic Leukemia and its Related Factors Using Competing Risks Model: A Retrospective Study from 2011 to 2019 in Northwestern Iran

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Abstract

Background: We aimed to evaluate the survival rate and define the prognostic factors in children with acute lymphoblastic leukemia (ALL).

Method: In this retrospective study, the data were extracted from the medical records of 176 children with ALL who referred to Motahari Hospital in Urmia from 2011 to 2019. Endpoints of overall survival study were event-free survival, disease-free survival, and recurrent mortality. Overall survival and disease-free survival were the time from diagnosis to death of any cause or recurrence. Event-free survival time was calculated as the distance from the date of diagnosis to the date of the last prevention with the first event. Non-recurrent mortality included all non-recurrent deaths. Data analysis was performed using a cause-specific hazard model.

Results: The mean age of the patients was 5.61 ± 3.56 years and the median of diagnosis of ALL to death was 3.47 ± 2.61 years. The 1-year, 3- year and 5-year probability of survival were 83.1%, 75.10%, and 68%, respectively. Sex, hemoglobin level, and hepatosplenomegaly were significant in univariate and multivariate analysis ($P < 0.05$).

Conclusion: The competing risks model was applied to identify the risk factors for all causes of death. The factors affecting the survival rate of patients in the model can be employed in making clinical decisions and proposing therapeutic protocols. Furthermore, it reduces the duration of response to therapy, thereby decreasing the rate of mortality in children.

Keywords: Acute lymphocytic leukemia, Cause-specific hazards, Childhood cancer, Competing risk

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Introduction

Acute lymphoblastic leukemia (ALL) is among the most prevalent cancers in children.[1] Annually, for every one hundred thousand people, 1 to 4.7 of people get the disease worldwide.[2] ALL accounts for about 25% of cancers in children under the age of 15 years.[3] The highest incidence of ALL is between 3 and 7 years of age, with about 75 % occurring prior to 6 years of age.[4] The survival rate of the disease has improved markedly over the past decades and the rate of recovery has increased to more than 90% in developed countries.[5] However, in developing countries, the success rates in the treatment of children with ALL have not been improved.[6] Therefore, in in the years 2010-2014, the highest survival rate was 93% belonging to Latin America, 80% in Costa Rica, and 76% in Argentina. In Colombia, Brazil, Shelby, and Peru, these children had a survival rate of less than 70%, while in Ecuador and Mexico it was less than 60%.[5] The difference in survival rates in different countries can be due to the differences in public health services,[7] socio-economic conditions and parental education,[8] poverty, and inequality.[9] Factors such as age at the time of diagnosis, gender, cytogenetics, size of liver and spleen, lymph node size, white blood cell count, central nervous system inflection, and response to primary treatment play an important role in determining the disease prognosis.[10-12] Thus, the survival rate of patients after diagnosis, treatment and its influencing factors are vital indicators in controlling and evaluating treatment methods.[13] In the analysis of survival data, the event of interest may occur for a variety of reasons, and the individual understudy experiences more than one type of event. In such circumstances, the best way to analyze data is to use competing risk models.[14, 15] In the last three decades, different methods have been introduced to analyze time failure data in the presence of competing risks. Prentice et al. proposed the use of standard models of survival analysis such as Cox regression in the cause-specific risk model.[16] Grover et al. (2014), used the cumulative incidence function to estimate the probability of death and the cause-specific and sub-distribution hazards models to evaluate the effect of the covariate on the cumulative incidence.[17] In the presence of competitive risks, standard statistical methods cannot be used for analysis. Different approaches have been used to analyze competing risks and the decision to choose the type of analysis depends on the study objectives. The cause-specific risk model is used for the etiology and if the purpose of the study is predictive, the sub-distribution risk model should be applied.[18] The present study is an attempt to determine the 5-year survival time and the factors influencing the survival of patients in the presence of competitive risks using a cause-specific model in children with ALL.

Methods

In the presence of competitive risks, standard statistical methods cannot be used for analysis. Different approaches have been used to analyze competing risks and the decision to choose the type of analysis depends on the objectives of the study. In this retrospective study, the medical records of 176 children under 15 years of age with ALL from April 2011 to March 2019 who were referred to Motahari hospital in West Azerbaijan province were studied. Of note, the only cancer referral center for pediatric leukemia in West Azerbaijan province is Shahid Motahari Medical Center in Urmia. The Ethics Committee of the Urmia University of Medical Sciences approved this study as retrospective study, in which in case of anonymous nature can be done; therefore, there was no need to obtain informed consent of the patient. In fact, this study had not intervention and it was kind of observational study (IR.UMSU. REC.1397.151).

Existing information was extracted from the patients' medical records and in case of incomplete records, telephone contact and interviews with the patient's family were conducted. The information was only available to researchers in the study and the names of the individuals were withheld. Inclusion criteria were a medical record of over 8 years (2011-2019). Individuals who were not native to West Azerbaijan province were excluded from the study. Prognostic factors

Table 1. Descriptive analysis of prognostic factors

Variable		Frequency (%)
Age	≤10 years	150(85.2)
	>10 years	25(14.2)
	Missing	1(0.6)
Sex	Girl	81(46)
	Boy	95(54)
Locate	City	88(50)
	Village	87(49.4)
	Missing	1(0.6)
Blood group	A	58(33)
	B	20(11.4)
	AB	10(5.7)
	O	54(30.7)
	Missing	34(19.2)
Family history	Yes	40(22.8)
	No	118(67)
	Missing	18(10.2)
WBC	>50000	46(26.1)
	≤50000	130(73.9)
T (9.22)	Positive	4(2.3)
	Negative	172(97.7)
T (1.19)	Positive	1(0.6)
	Negative	175(99.4)
Risk of disease	High	92(52.3)
	Standard	54(30.7)
	Low	27(15.3)
	Missing	3(1.7)
Immunophenotyping	Mature B-cells	6(3.4)
	Precursor B-cells	100(56.8)
	Precursor T-cells	18(10.3)
	Missing	52(29.5)
Response to treatment	Complete remission in 28th day	138(78.4)
	No complete remission in 28th day	9(5.1)
	No complete remission	22(12.5)
	Missing	7(4)
Rheumatoid signs	Yes	-
	No	170(96.6)
	Missing	6(3.4)
Hepatosplenomegalia ≥2 cm	Yes	64(36.4)
	No	106(60.2)
	Missing	6(3.4)
Lymphadenopathy≥2 cm	Yes	64(36.4)
	No	106(60.2)
	Missing	6(3.4)
Fever, cough, and diarrhea	Yes	52(29.5)
	No	118(67.1)
	Missing	6(3.4)
Weakness and loss of anorexia	Yes	63(35.8)
	No	107(60.8)
	Missing	6(3.4)
Testicular swelling	Yes	5(2.8)
	No	165(93.8)
	Missing	6(3.4)
Bleeding	Yes	36(20.5)
	No	134(76.1)

Table 1. Descriptive analysis of prognostic factors

Variable		Frequency (%)
	Missing	6(3.4)
Lower extremity pain - Abdominal pain		
	Yes	44(25)
	No	126(71.6)
	Missing	6(3.4)
CNS	Positive	45(25.6)
	Negative	123(69.9)
	Missing	8(4.5)
Testis	Positive	8(4.5)
	Negative	160(91)
	Missing	8(4.5)
Radiotherapy	Yes	71(40.3)
	No	97(55.2)
	Missing	8(4.5)
Status	First recurrence	28(15.9)
	Death	49(27.9)
	Alive	99(56.2)
Quantitative variables	BMI (kg/m^2)	15.732.47
	Platelet(mcL)	70857.3378540.89
	Hemoglobin (g/dl)	7.272.79
	LDH (U/l)	1551.391970.90

WBC: White blood cell; CNS: Central nerve system; BMI: Body mass index; LDH: Lactate dehydrogenase

included in the analysis were age, gender, place of residence, patient body mass index, platelet count, hemoglobin level, LDH rate, blood group, family history, white blood cell count, cytogenetic

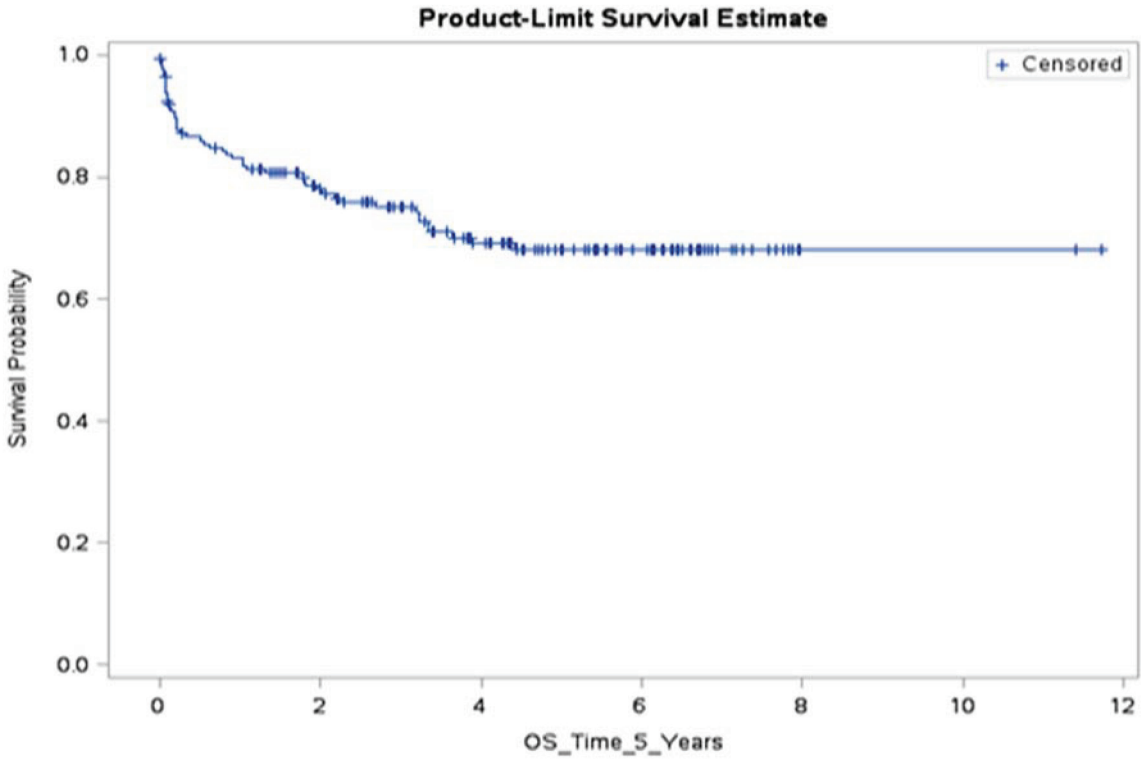

Figure 1. The cumulative incidence curve for OS non-event survival in which there were no significant differences between OS survival and non-event survival over time.
OS: Overall survival

Table 2. Univariable and multivariable cox proportional hazard models for DFS cause

Variables		HR (%75 CI)	*P* value
Age	≤10 years	0.94(0.50-1.75)	0.91
	>10 years	-	-
Sex	Female	0.36(0.21-0.62)	0.03
	Male	-	-
Locate	City	1.20(0.77-1.85)	0.63
	Village	-	-
BMI		1.12(1.03-1.22)	0.09
Platelet		1(-)	0.27
Hemoglobin		1.17(1.08-1.27)	0.01
LDH		1(-)	0.78
Blood group	A	0.63(0.37-1.07)	0.31
	B	0.88(0.41-1.86)	0.84
	AB	0.45(0.13-1.52)	0.45
	O (RL)	-	-
Family history	Yes	1.08(0.46-2.52)	0.84
	No (RL)	-	-
	>50000	1.79(1.14-2.83)	0.13
WBC	≤50000	-	-
t(9.22)	Positivet	3.35(1.02-10.94)	0.24
	Negative	-	-
t(1.19)	Positive	16.61(4.94-55.87)	0.007
	Negative	-	-
Risk of disease	High	4.76(2.04-11.12)	0.03
	Standard	0.47(0.15-1.50)	0.45
	Low(RL)	-	-
Immunofenotype	Mature B-cells	2.43(0.75-7.83)	0.38
	Precursor B-cells	0.91(0.37-2.21)	0.90
	Precursor T-Cells	-	-
Response to treatment	Complete remission in 28th day	0.10(0.06-0.17)	<0.0001
	No complete remission in 28th day	0.16(0.04-0.56)	0.08
	No complete remission	-	-
Hepatosplenomegalia≥2 cm	Yes	0.30(0.16-0.56)	0.02
	No	-	-
Lymphadenopathy≥2 cm	Yes	0.53(0.26-1.08)	0.30
	No	-	-
Fever, cough, and diarrhea	Yes	0.65(0.36-1.17)	0.40
	No	-	-
Weakness and loss of appetite	Yes	0.40(0.22-0.71)	0.07
	No	-	-
Testicular swelling	Yes	11.53(6.38-20.83)	<0.0001
	No	-	-
Bleeding	Yes	0.54(0.26-1.09)	0.31
	No	-	-
Lower extremity pain	Yes	0.65(0.36-1.16)	0.39
Abdominal pain	No	-	-
CNS	Positive	2.94(1.87-4.64)	0.006
	Negative	-	-
Testis	Positive	10.33(6.29-16.96)	<0.0001
	Negative	-	-
Radiotherapy	Yes	0.47(0.34-0.67)	0.01
	No	-	-

BMI: Body mass index; LDH: Lactate dehydrogenase; CNS: Central nerve system; DFS: Disease-free survival; WBC: White blood count; HR: Hazard ration; CI: Confidence interval; RL: Reference line

abnormalities, disease risk, immunophenotype, response to treatment, clinical symptoms including bone and joint pain and inflammation, hepatosplenomegaly greater than 2 cm, lymphadenopathy higher than 2 cm, fever, cough, diarrhea, weakness, anorexia suppression, testicular swelling, bleeding, abdominal pain, lower limb pain, CNS involvement, and radiotherapy. The patient profile was descriptively reported. The competitive regression model of the specific cause was processed for factors affecting the survival of ALL patients. Endpoints of the study were relapse-free death. Effect-free survival (EFS) and disease-free survival (DFS) were the time from diagnosis to death of any cause or recurrence. Event-free survival was calculated as the interval between the date of diagnosis and the date of the last follow-up to the first event. Non-recurrent mortality included recurrent non-recurrent deaths. The Kaplan-Meier method was used to estimate EFS and overall survival (OS) probabilities. Non-relapse mortality (NRM) was a competing risk for DFS. Unavailable and multivariable analysis was performed using the cause-specific competing risk model for DFS and NRM. Multivariable model selection in the model was done with a backward method for selecting the features with the highest prognostic value. The assessment proportional hazard assumption was performed using the score process plot and Kolmogorov-type supremum test in the cox PH model (Significant level=0.05). Computations were performed using SAS (version 9.4; SAS Institute Inc, Cary, NC, USA). The significant level for univariable and multivariable analyses was assigned 0.25 and 0.10, respectively.

Results

The present study included 176 children with ALL. Overall, 85% of the patients were less than 10 years old and 15% were more than 10 years old. 95 patients were boys and 81 patients were girls. About 52.3% of the patients were at high risk, 30.7% at standard risk, and 15/3% at low risk. Moreover, 25.6 and 69.9% of the children had and did not have CNS, and 40.3 and 55.2% were treated with radiation or not. Table 1 shows the other clinical and demographic characteristics of the patients. The OS rates of 1-, 3-, and 5-year-old children with ALL were 83.1 [%95 confidence interval (CI) (76.6, 87.9)], 75.1 [%95 CI (67.6, 81.0)] and 68% [%95 CI (59.6, 75.0)], respectively. Also, 1-, 3-, and 5-year survival rates of these children were 82.5 [%95 CI (76, 87.4)], 73.3 [%95 CI (65.8, 79.4)] and 65.3%

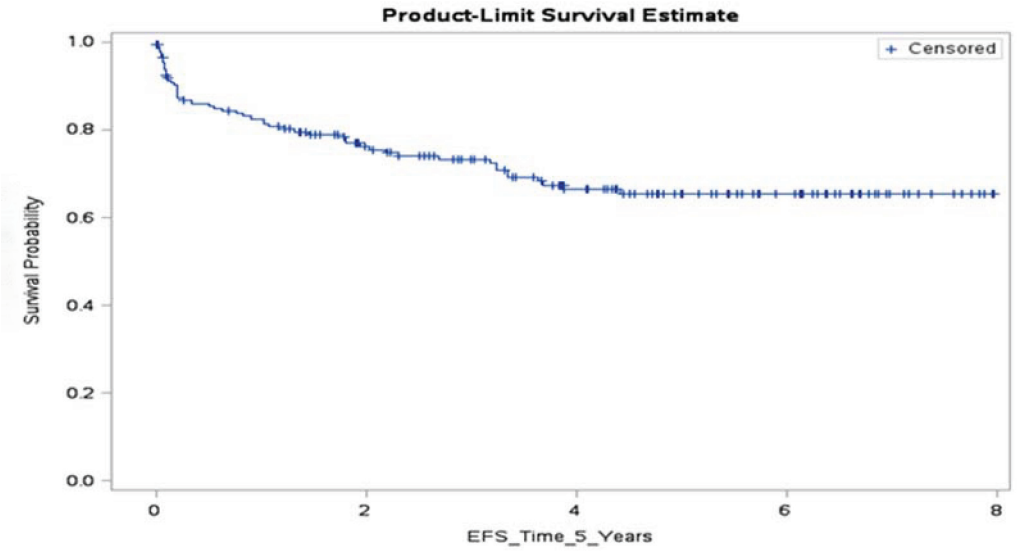

Figure 2. This figure shows the probability of cumulative risk of DFS overtime.
DFS: Disease-free survival

[%95 CI (56.8, 72.5)], respectively. The cumulative incidence curve for OS and non-event survival is shown in figure 1. There was no significant difference between OS and non-event survival over time.

According to table 2, based on the results of the univariate analysis of gender prognosis factors, patient body mass index, hemoglobin level, white blood cell (WBC), response to treatment, clinical symptoms of hepatosplenomegaly, anorexia, testicular swelling, as well as CNS involvement, testicular involvement, and radiotherapy were significantly associated with recurrence events in children. Accordingly, girls had a better prognosis for DFS compared with children hazard ratio (HR) (female to male= 0.36; 75% CI: (0.21, 0.62)). The increase in patients' body mass index increased the recurrence in cidencein children by 12% (HR = 1.12; 75% CI: 1.03, 1.22). Increased patient hemoglobin had a poor prognosis for pediatric DFS (HR = 1.17; 75% CI: (1.08, 1.22)). Children with a WBC above 50000 compared with children with a WBC of 500000 had a higher recurrence rate of 79% (HR=1/79; 75%CI; (1.14, 2.83)). Children with t (9. 22) and t (1.19) had a poorer prognosis than t (1.19) t(9.22). Children with a high disease risk were 4.76 times more likely to have a recurrence incidence than children with a low risk (HR = 4.76; 75% CI: (2.04, 11.12)). Children responding to treatment on the 28th day (HR = 0.10; 75% CI: (0.06, 0.17)) and those responding to no treatment on the 28th day (HR = 0.16; 75% CI: (0.04, 0.56)) had 90% and 82% lower risk of recurrence than children who did not respond to treatment, respectively. Children with hepatosplenomegaly greater than 2 cm had a 70% lower risk of recurrence (HR=0.30; 75% CI: (0.16, 0.56)). Children with weakness and loss of anorexia had a 60% lower risk of recurrence (HR = 0.40; 75% CI: (0.22, 0.71)). Children with testicular swelling had a poor prognosis for DFS (HR = 11.53; 75% CI: (6.38, 20.83)). Children with (CNS) involvement had a poorer prognosis for DFS compared with children without CNS involvement (HR Positive to Negative = 2.94; 75% CI: (1.87, 4.64)), which was also true for testicular involvement variable (HR positive to negative = 10.33; 75% CI: (6.29, 16.96)). Children who received radiotherapy had a 53% lower risk of recurrence in comparison

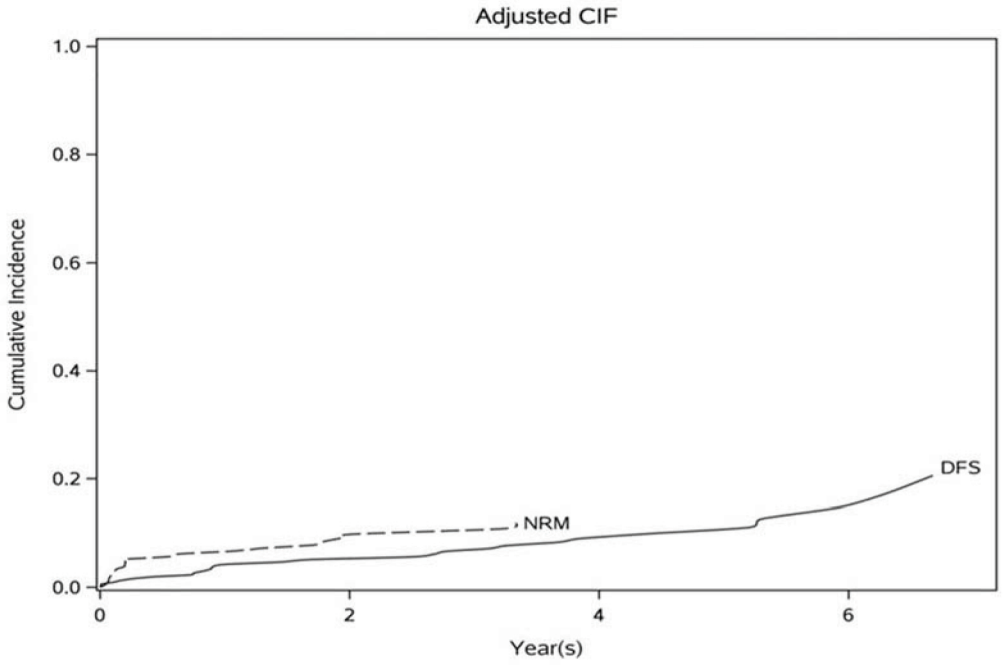

Figure 3. Risk (as adjusted CIF) of developing NRM and DFS, as seen NRM in the first three years was higher than the risk of recurrence.
CIF: Cumulative incidence function; NRM: Non-relapse mortality; DFS: Disease-free survival.

Table 3. Univariable and multivariable cox proportional hazard models for NRM cause

Variables		HR (%75 CI)	*P* value
Age	≥10 years	0.81(0.46, 1.43)	0.67
	>10 years	-	-
Sex	Female	1.56(1.02, 2.38)	0.22
	Male	-	-
Locate	City	1.30(0.85, 1.99)	0.47
	Village	-	-
BMI		1.04(0.96, 1.14)	0.50
Platelet		0.99(0.99, 1.01)	0.50
Hemoglobin		1.02(0.92, 1.08)	0.97
LDH		1.01(0.99, 1.01)	0.27
Blood group	A	0.82 (0.48, 1.42)	0.68
	B	1.86 (0.99, 3.41)	0.26
	AB	0.50(0.14, 1.68)	0.51
	O	-	-
Family history	Yes	0.23(0.10, 0.54)	0.049
	No	-	-
WBC	>50000	1.04(0.65, 1.68)	0.91
	≤50000	-	-
t(9.22)	Positive	1.67(0.22, 12.36)	0.61
	Negative	-	-
t(1.19)	Positive	0(0-NE[4])	0.99
	Negative	1.50(0.79, 2.83)	0.46
High risk of disease	Standard-	0.97(0.48, 1.97)	0.96
	Low	-	-
Immunophenotyping	Mature B-cells	0.54(0.15, 1.90)	0.57
	Precursor B-cells	0.59(0.33, 1.07)	0.31
	Precursor T-cells	-	-
Response to treatment	Complete remission in 28th day	0.10(0.06, 0.16)	<0.0001
	Complete remission in 28th day	0.38(0.18, 0.81)	0.14
	No complete remission	-	-
Rheumatoidsigns	Yes	NE[4]	NC
	No	-	-
Hepatosplenomegalia ≥2 cm	Yes	0.68(0.43, 1.07)	0.33
	No	-	-
Lymphadenopathy≥2 cm	Yes	0.58(0.31, 1.07)	0.31
	No	-	-
Fever, cough, and diarrhea	Yes	1.55(1.01, 2.39)	0.23
	No	-	-
Weakness and loss of anorexia	Yes	1.84(1.21, 2.80)	0.09
	No	-	-
Testicular swelling	Yes	0(0, NE[4])	0.99
	No	-	-
Bleeding	Yes	0.59(0.32, 1.10)	0.33
	No	-	-
Lower extremity pain	Yes	0.95(0.59, 1.54)	0.91
Abdominal pain	No	-	-
CNS	Positive	0.86(0.52, 1.42)	0.73
	Negative	-	-
Testis	Positive	0(0, NE[4])	0.98
	Negative	-	-
Radiotherapy	Yes	0.22(0.12, 0.40)	0.003
	No	-	-

BMI: Body mass index; LDH: Lactate dehydrogenase; WBC: White blood cell; CNS: Central nerve system; NRM: Non-relapse mortality; HR: Hazard ratio; CI: Confidence interval

with those who did not undergo radiotherapy (HR = 0.47; 75% CI: (0.34, 0.67)).

According to table 3 based on the results of univariate analysis, the prognosis factors of gender, family history, response to treatment, mediastinal mass, fever and cough and diarrhea, weakness and loss of anorexia and radiotherapy were significantly correlated with the incidence of death prior to the first relapse of children. Accordingly, girls had a better prognosis for NRM than boys (HR female to male= 0.64; 75% CI: (0.41, 0.97)). Children with a family history also had a good prognosis for NRM (HR = 0.23; 75% CI: (0.101, 0.54)). Children responding to treatment on the 28th day (HR = 0.10; 75% CI: (0.06, 0.16)) and children responding to no treatment on the 28th day (HR = 0.38; 75% CI: (0.18, 0.81)) had 90 and 62% lower risk of recurrence than those who did not respond to treatment, respectively. Children with fever, cough, and diarrhea had a 55% higher risk of dying without recurrence compared with children without these symptoms (HR = 1.55; 75% CI: (1.01, 2.39). Children with weakness and reduced anorexia had an 84% higher risk of dying without recurrence compared to children without these symptoms (HR = 1.84; 75% CI: (1.21, 2.80)). Children who received radiotherapy had a better prognosis for NRM in comparison with those without radiotherapy and had a 78% lower risk of death without recurrence (HR = 0.22; 75% CI: (0.12-0.40)).

As can be seen in figure 2 and 3, the probability of cumulative occurrence in DFS for 1, 3, 5 years reached 0.04, 0.066, and 0.099, respectively. Accordingly, the cumulative risk for ALL recurrence in 1, 3, and 5 years was 0.04, 0.066 and 0.099, respectively. For NRM, the cumulative probability of 1 and 3 was 0.066 and 0.108, respectively; thus, the cumulative risk for NRM in years 1 and 3, when there is also a first recurrence, was 6.6 and 10.8, respectively. Therefore, the risk of developing NRM in the first three years was higher than the risk of recurrence.

Discussion

This study aimed to apply Cox regression model in order to analyze the consequences of leukemia in West Azerbaijan province and showed that 1, 3, and 5-year survival rate was 83.1%, 75.10%, and 68%, respectively. In addition, gender, hemoglobin, and hepatosplenomegaly were significant predictorsin univariate and multivariate analysis. In this study, we tried to assess some of the factors impacting the prognosis of ALL patients, including age, sex, WBC, platelet count, and recurrence rate in the five-year survival of this group of patients. Leukemia is one of the most common cancers, accounting for about 3% of all cancers in developing and developed countries.[19-21] In the present study, family history had a significant effect on survival rate, and in some studies, family history was also implicated in leukemia survival, particularly acute myeloid leukemia (AML).[20, 21] As a result, there have been various reports from patients with a family history that the role of this agent in leukemia cancer is unclear.[21] The survival rate of patients with leukemia cancer decreased with age, which is in line with other studies.[22, 23] In the present study, patients with no history of relapse had 1-, 3-, and 5-year survival rates of 83.1%, 75.10%, and 68%, respectively, and those with a history of relapse had rates of 82.5%, 73.3%, and 65.3%, respectively. Mean survival was not significantly different between the two groups ($P > 0.001$). In Cox multivariate analysis, sex variables, hemoglobin level, disease risk and hepatosplenomegaly greater than 2 cm were significantly associated with disease survival ($P < 0.001$). Increased hemoglobin reduced the history of recurrence in children by 17%. Children at high risk of disease were 21.46 times more likely to have recurrence compared with those at low risk, and children with hepatosplenomegaly greater than 2 cm had 84% lower recurrence rate. Girls had a lower recurrence history than male children. For non-recurrence event in the classified Cox model, variables of gender, family history of disease and response to treatment were significantly associated with NRM ($P < 0.001$).

In confirmation of our study results, many

researchers have shown that hepatomegaly, splenomegaly, and lymphadenopathy can be detected in up to half of patients on presentation. Hepatomegaly occurs due to the sequestration of platelets and lymphocytes in the spleen and liver, and as the white blood cells are not typical, the spleen reacts to them by trying to remove them from the blood.[24-26]

In each of these variables, girls had a higher risk of dying without recurrence than boys, with constantly considering the effect of other variables in the final model. Children who did not respond to treatment on day 28 had 91% lower risk of dying before relapse than those with no response to treatment. In this study, age and sex did not show any significant relationship with ALL 5-year survival rate.[27] Almasi et al. conducted a study to determine the survival rate of acute leukemia in children based on recurrence status at Shahid Fahighi Hospital in Shiraz from 2004 to 2009. They found that 1- and 5-year survival rates in patients with no history of recurrence were 96.9% and 76.0%, whereas the survival rates in patients with a history of recurrence were estimated to be 82.4 and 28.6%, respectively, indicating a significant relationship between the history of relapse and survival rate.[28] In our study, however, 1- and 5-year survival rates among 75.11 and 68% relapsing patients were estimated to be significantly lower in the aforementioned areas. Also, 1- and 5-year survival rates in non-recurrent patients were estimated to be 73.3% and 65.3%, which were lower in relapsed patients. Five-year survival rates in this study were much lower than those in high-income countries.[29-31]

Feltbower et al. conducted a study on 1177 patients aged 0 to 14 years with blood malignancies diagnosed between 1974 and 2003 in Yorkshire, England. According to their findings, the five-year survival rate was 46% in patients with recurrence and 79% in patients without a history of recurrence.[30] In our study, the five-year survival rate among relapsed patients was 68%, which is significantly higher than in the aforementioned areas. However, the five-year survival rate in patients without a history of recurrence was estimated to be 65.3, often less than other centers.

Zarei Far et al. reported that in their study, the five-year cumulative cancer survival rate was 53.3 ± %55,[31] which is higher than the reported percentage. The researchers also reported that survival rates in both males and females were relatively similar, which is different from our study. In terms of gender, our study is similar to that of Feltbower et al. with a lower recurrence rate in females than in males.[30]

Almasi, Zarei Far and Basta reported no significant relationship between the two variables regarding the variable role of hemoglobin and disease recurrence. Nonetheless, the results of our study showed that an increase in hemoglobin levelled to a reduction in the recurrence of the disease, which is negligible according to similar studies.[28, 29, 31]

In their study, Souza et al. investigated the association between acute leukemia and hepatosplenomegaly, reporting a significant relationship between the two variables.[19] Our results confirmed that the recurrence rate decreased with the increase in size to over 2 cm.

The limitations of this study were incomplete data related to recurrence time and number of recurrences in some cases. Details of the biological and molecular genetic information of the patients were also unavailable. Biological and molecular genetic information can be a useful tool for determining the survival rate following relapse. For instance, chromosomal translocation of q23 11 and the Philadelphia chromosome in ALL suggest poor prognosis and are associated with poor patient survival. However, the 21:8 chromosomal translocations, which are actually the fusion of the AML1-TEL genes, provide a favorable prognosis in AML patients. Due to the limitations of the current study, further studies with more complete information from these patients are recommended.

Conclusion

Competing-risks analysis extends the ability of ordinal survival analysis to data that have multiple causes of failure. Natural interpretation was attained through cause-specific approach.

According to the cause-specific model, sex, hemoglobin level and hepatosplenomegaly are the most important associated risk factors for ALL. Therefore, the factors affecting the survival rate of patients in the model can be employed in making clinical decisions and proposing therapeutic protocols.

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Conflict of Interest

None declared.

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