

SURVIVAL AND DEMOGRAPHIC FEATURES IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA



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ABSTRACT

Background

Acute lymphoblastic leukemia (ALL) is a malignant blood cancer of T-cell or B-cell lineages.

Objectives

The aim was to obtain local data on the demographic features of pediatric patients with ALL and correlate them with a five-year survival rate.

Patients and Methods

A retrospective cohort study was performed on 94 ALL pediatric patients aged 1-14 admitted to the Hiwa Hospital from 2014 to 2016. The diagnostic methods, clinical features, and histological and biochemical parameters were reviewed. Further, a five-year survival rate was assessed.

Results

The mean±SD (standard deviation) of patients' ages at diagnosis was 5.2±3.1 years, ranging from 1 to 14. Males were 57.4%, and females were 42.6%, with a male-to-female ratio of (1.35:1). Most patients (61.7%) suffered from the low-risk (A), and the majority of patients (90.4%) were in remission. The five-year survival rate was 80.9%. The associations of age groups, gender, white blood cell (WBC) groups, risk groups, and post-induction status with a five-year survival rate were insignificant (p-values of >.05). The association of immunophenotyping with the five-year survival rate was statistically significant (p-value = .014).

Conclusion

The 5-year survival rate was 80.9% in the current study. Further, although the frequency of some characteristics was more than others, the associations of the patient characteristics with the five-year survival rates were insignificant, except for the association of the five-year survival rate with immunophenotyping which was significant.

Keywords: *Acute Lymphoblastic Leukemia (ALL); Children; Demographic features; five-year survival rate; Pediatrics; Slemani.*

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INTRODUCTION

Cancer is the primary cause of death in pediatric age groups globally, and the age-standardized incidence rate below 15 years of age is 14.1 per 100000 per year ⁽¹⁾. Further, the most common childhood cancer is leukaemia worldwide ^(2,3). Acute lymphoblastic leukaemia (ALL) constitutes 76% of all leukaemia cases and 43% of all deaths from childhood leukaemia in the USA ⁽³⁾. About 20% of all tumours before age 20 are ALL ⁽²⁾. However, the 5-year survival rate improved from 10% to 90% in the 1960s and 2000s, respectively ^(2,4). An overall 5-year survival rate of childhood ALL nowadays exceeds 90% in high-income countries ⁽⁵⁾.

Acute lymphoblastic leukaemia (ALL) is a cancer of the blood originating from either T-cell or B-cell lineages with differences in the heterogeneity of its subtypes regarding chromosomal derangements, immunophenotypes, and responses to therapy ⁽³⁾.

Age at diagnosis was considered a significant prognostic factor for the incidence and survival rate of childhood ALL ^(3,6). For instance, the lowest survival rate was found for patients diagnosed during infancy, followed by children diagnosed between 15-19 years old ^(3,6). However, children aged one to nine had more chances of surviving ⁽³⁾. These variations are partly due to the biological differences of the disease; older ALL children have more T-cell phenotype but less hyper diploidy or translocation of ETV6-RUNX1 ⁽⁶⁾.

Furthermore, other factors were mentioned in the literature that influences the survival rate of childhood ALL, including gender, ethnicity, primary cancer site, and therapy ⁽³⁾. Besides, non-Hispanic Caucasians and the female gender had more favourable survival rates than the other ⁽³⁾. To the best of our knowledge, the studies which have been done in Kurdistan Region/Iraq on the same topic are as follows: one study found a 3-year survival rate of 71.98% for children ⁽⁷⁾, another study found a 5-year survival rate of 49% for adults ⁽⁸⁾, and another study focused on chronic lymphocytic leukaemia (CLL) ⁽⁹⁾. Also, we found another study in the Kurdistan Province of Iran that focused on adult and pediatric ALL and acute myeloid leukaemia (AML); they found a 5-year survival rate of 83% in the children ⁽¹⁰⁾.

Therefore, the current study aimed to obtain local data in the Slemani/Kurdistan Region on demographic features of pediatric patients with ALL and correlate them with a 5-year survival rate from the date of the diagnosis.

PATIENTS AND METHODS

A retrospective cohort study was performed on 94 pediatric patients admitted to the Hiwa Hospital from January 1st, 2014, to December 31st, 2016. The patients were randomly selected by using a simple random sampling method.

The Ethical Committee of the College of Medicine/University of Slemani approved the study proposal, and a formal acceptance letter was obtained from the Hiwa Hospital before starting the study. Also, the patients' companions gave informed consent for inclusion in the study.

The inclusion criteria included patients of both genders aged between 1-14 years diagnosed with ALL by bone marrow aspiration (BMA) and biopsy and flow cytometry. However, the exclusion criteria included ALL and Down syndrome patients and ALL secondary to other malignancies due to chemotherapy and radiotherapy.

Detailed clinical features, such as age and gender, were recorded. Reviews of the diagnostic methods, either BMA and biopsy or flow cytometry, clinical features, and histological and biochemical parameters, were performed, and the patients were classified into three risk groups. Further, a five-year survival rate was assessed.

Sample size estimation was performed using the "GPower 3.1" program, which yielded 94 samples; thence, the sample size of 94 patients was obtained when the effect size was 0.46, a P-value of ≤ 0.05 , and the study power of $>95\%$ was selected. Moreover, the "IBM SPSS Statistics version 26" software was used to analyze the data, and descriptive and inferential statistics were used. Further, a P-value of ≤ 0.05 was considered a statistically significant association. Besides, Pearson Chi-Square was used to determine the significance of the association between categorical independent and dependent variable pairs. Also, the Kaplan-Meier test was used to assess the survival rates.

RESULTS

The mean \pm SD (standard deviation) of patients' ages at diagnosis was 5.2 ± 3.1 years, ranging from 1 to 14. Besides, the gender of the patients was 54 (57.4%) males and 40 (42.6%) females, with a male-to-female (M: F) ratio of (1.35:1).

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The majority of patients (85.1%) presented with fever, followed by pallor (69.1%), bone pain (63.8%), bleeding (48.9%), and organomegaly (48.9%). Also, all the patients (100%) were diagnosed by both flow cytometry and BMA plus biopsy.

The laboratory findings of the enrolled patients are shown in Table 1. Most patients (61.7%) suffered from the low-risk group (A), and the majority of patients (90.4%) were in remission. Also, most patients (35.1%, 33%, and 21.3%) had blood groups of A+, O+, and B+, respectively (Table 2). Although the association between the age groups and survival was statistically insignificant (p-value = .513), most deaths (10.6%) occurred between the ages of five and nine. The distributions of the survival and age groups are shown in Figure 2. Although the association of the gender of the patients with survival was statistically insignificant (p-value = .055), most deaths (14.9%) occurred in males. The distributions of the survival and gender of the patients are shown in Figure 3. Although the association of WBC groups with survival was

statistically insignificant (p-value = .745), most deaths (16%) occurred in WBC counts of between 10000-50000.

The distributions of the survival and WBC groups are shown in Figure 4. Although the association of risk groups with survival was statistically insignificant (p-value = .121), most deaths (10.6%) occurred in low-risk groups. The distributions of the survival and risk groups are shown in Table 3 and Figure 5. Although the association of post-induction status with survival was statistically insignificant (p-value = .387), most deaths (14.9%) occurred in the remission group. The distributions of the survival and the post-induction status are shown in Table 4 and Figure 6. The association of immunophenotyping with survival was statistically significant (p-value = .014), and most deaths (13.8%) occurred in the B-cell group. The distributions of the survival and immunophenotyping are shown in Figure 7.

Table 1. Distribution of the blood and serum parameters of the enrolled patients.

Parameters	Mean	Median	SD	Minimum	Maximum
WBC count (per microliter)	39139.4	9800.0	84175.6	200.0	500000.0
Haemoglobin (g/dl)	8.6	8.3	2.2	3.4	14.0
CRP (mg/dL)	21.1	7.0	58.1	0.0	432.0
Platelet count (per microliter)	80344.7	52500.0	88275.9	5000.0	444000.0
ESR (mm/hr)	61.0	55.0	38.4	2.0	174.0
Bone marrow blast (%)	85.1	88.0	11.2	45.0	99.0

CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; SD = standard deviation; WBC = white blood cells.

Table 2. Characteristics of patients with ALL.

Characteristics	Frequency	Percent	
Risk group	Low-risk group (A)	58	61.7
	Intermediate-risk group (B)	31	33
	High-risk group (C)	5	5.3
Post-induction status	In remission	85	90.4
	Not in remission	9	9.6
Blood groups	A+	33	35.1
	A-	2	2.1
	B+	20	21.3
	B-	1	1.1
	AB+	3	3.2
	AB-	1	1.1
	O+	31	33
	O-	3	3.2
Total	94	100	

The mean±SD survival of the patients was 5.5±2.4 years, ranging from 0 to 8 years. The 5-year survival rate was 80.9% (Figure 1).

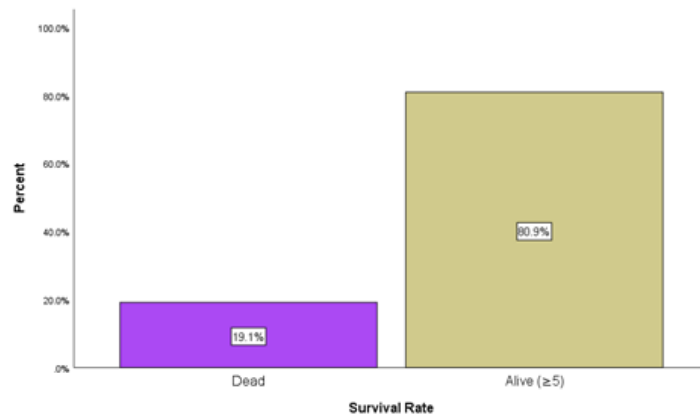


Figure 1. A five-year survival rate from the diagnosis.

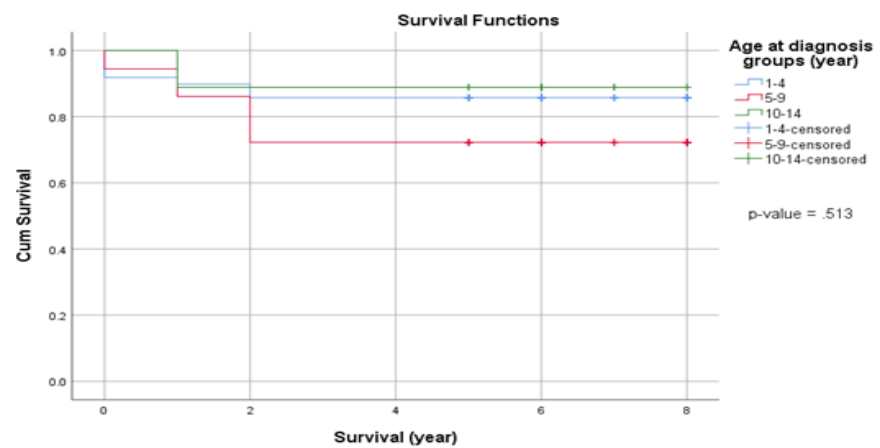


Figure 2. Association of age groups at diagnosis and a five-year survival rate.

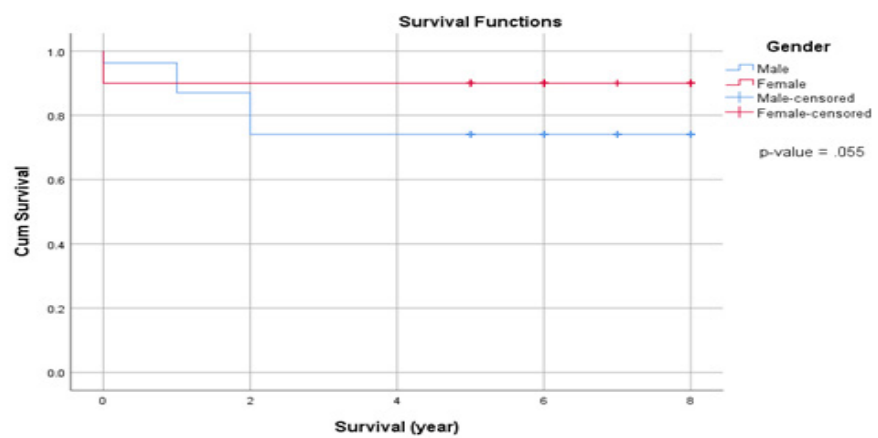


Figure 3. Association of the gender of the patients and a five-year survival rate.

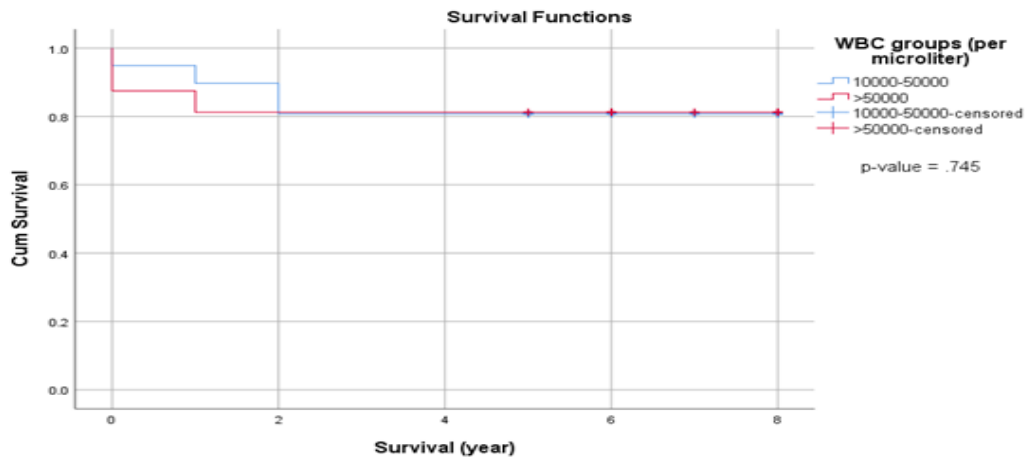


Figure 4. Association of WBC groups and a five-year survival rate.

Table 3. Case processing to measure the association of risk groups with the five-year survival rate.

Case Processing Summary				
Risk groups	Total N	N of Events	Censored N	Censored Percent
Low-risk group (A)	58	10	48	82.8%
Intermediate-risk group (B)	31	5	26	83.9%
High-risk group (C)	5	3	2	40.0%
Overall	94	18	76	80.9%

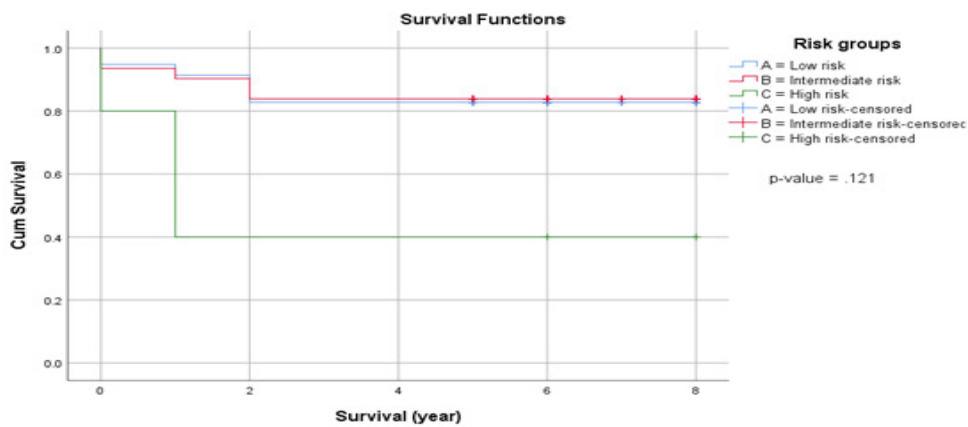


Figure 5. Association of risk groups and a five-year survival rate.

Table 4. Case processing to measure the association of post-induction status with the five-year survival rate.

Case Processing Summary				
Post-induction status	Total N	N of Events	Censored	
			N	Percent
In remission	85	14	71	83.5%
Not in remission	9	4	5	55.6%
Overall	94	18	76	80.9%

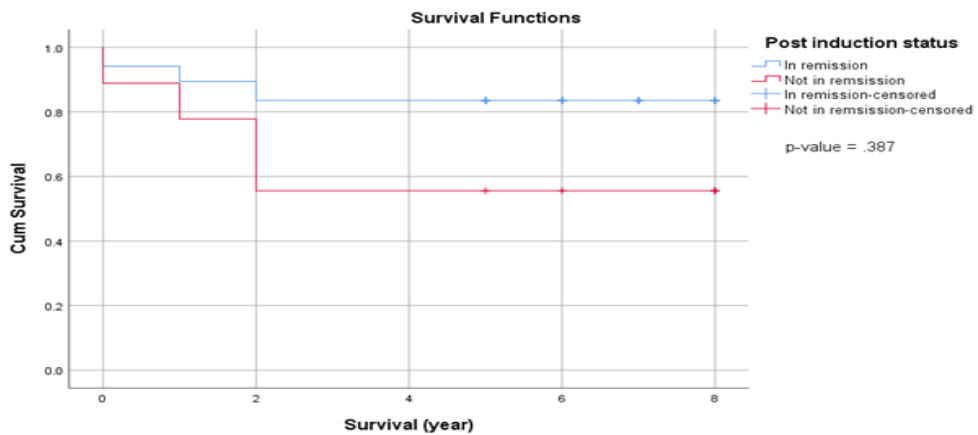


Figure 6. Association of post-induction status and a five-year survival rate.

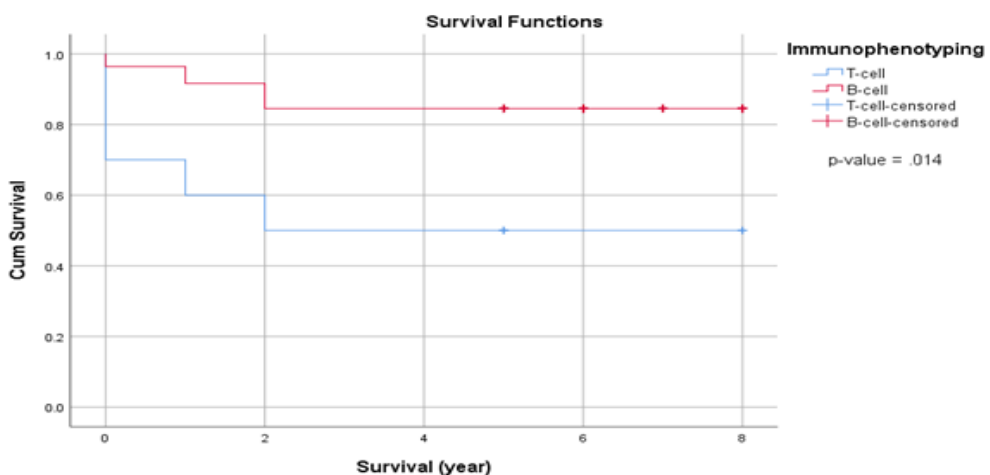


Figure 7. Association of immunophenotyping and a five-year survival rate.

DISCUSSION

In the current retrospective study, conducted on 94 pediatric patients proven to have ALL by BMA and biopsy and flow cytometry in Slemani province of Kurdistan Region of Iraq, the 5-year survival rate was 80.9% for ages one to 14 years. Further, we focused on the age and gender of the patients, clinical and laboratory findings, and a 5-year survival rate. The Kaplan-Meier correlation between the findings and the 5-year survival rate was also obtained.

The mean±SD of ages at diagnosis was 5.2±3.1 years, ranging from one to 14 years. The age of the patients in the current study was slightly lower than the pediatric patients' ages in the studies performed in Turkey⁽¹¹⁾ and the Kurdistan Region of Iraq⁽⁷⁾; the mean±SD of ages was 11.3±3.8 (ranging from 5.5-18) and 6.9±2.9 (ranging, 1.5–18) years, respectively. However, our finding was similar to ages in the Kurdistan Province of Iran; 5.2±3.51 (ranging from 0-14), except for selecting below one year⁽¹⁰⁾. The variability of ages at the diagnosis in the studies is due to the differences in their patient selections, we selected ages from one to 14 years, but others selected differently. Similarly, the most frequent age group was between one to four in the study of Al Odda et al.⁽⁷⁾ in the Kurdistan Region and Alecsa et al.⁽¹²⁾ in Romania, the same as our result. Al Odda et al.⁽⁷⁾ selected their patients in the same population as the current study; thus, similarities between the studies may be due to that. However, the study by Alecsa et al.⁽¹²⁾ in Romania collected all their patients from a population of nearly one million children for six consecutive years for ages one to 17 years; although the explanation for the same is complicated, our similarity may be due to our origin of Kurds and Romanian as Indo-European Family, as the Encyclopedia Britannica mentioned⁽¹³⁾.

Although the male gender was slightly higher in frequency in the current study than the female gender; 57.4% males and 42.6% females, with a male-to-female ratio of 1.35:1, this ratio was slightly less than what has been found in the literature; it was 1.7:1 and 1.73:1 in the studies done by Yasmeen et al.⁽¹⁴⁾, and Al Odda et al.⁽⁷⁾, respectively. The minor variation that was present in the preceding two studies with the current study concerning gender may be due to the variation of sample sizes and age span selection of their patients; the study of Yasmeen et al.⁽¹⁴⁾ selected 611 patients aged three months to 15 years, and the study of Al Odda et al.⁽⁷⁾ selected 257 patients aged from one to 18 years.

Most patients (89.4%) were diagnosed with B-cell immunophenotype of ALL in the current study. Our findings were in accordance with the results found in Japan, which showed 85-90% of B-cell lineage for their pediatric patients⁽¹⁵⁾. Besides, most patients (61.7%) in the current study fell into the low-risk group, followed by the intermediate-risk group (33%), and only 5.3% of the patients fell into the high-risk group. Further, the risk groups' frequencies were near the ones found in the literature⁽⁷⁾.

The 5-year survival rate in the current study was 80.9%. Our findings showed improvement compared to the study performed by Al Odda et al.⁽⁷⁾ in the same locality, who found a 3-year survival rate of about 72% for patients from 2007 to 2013; however, it was slightly less than the 5-year survival rate of 90.4% in the United States of America (USA) and Canada⁽¹⁶⁾. The study by Hunger et al.⁽¹⁶⁾ chose patients aged zero to 22. Although they did the study until 2005, they had more advanced molecular assessments of the risk groups, thence, more advanced therapies accordingly. Therefore, the current study was done in a developing country willing to catch the more advanced methods to improve patient outcomes.

We then performed Kaplan-Meier and Pearson Chi-Square tests to know the associations between the patient's findings and a 5-year survival rate. However, we could not find any statistically significant associations between the survival rate and patients' findings, except for the association of immunophenotyping with survival rate, which was statistically significant (p-value = .014). Although the frequency of B-cell ALL patients was higher than T-cell ALL patients, the survival rate of patients with B-cell ALL was much more (84.5%) than that of patients with T-cell ALL (50%) (Table 9 and Figure 7). Further, the associations of age groups, gender, WBC groups, risk groups, and post-induction status with the survival rate were statistically insignificant (p-values of >0.005).

In comparison, Al Odda et al.⁽⁷⁾ found a statistically significant association (p-value of .003) of gender with the 3-year survival rates favouring the female gender. They suggested that testicular relapse due to the testicular-blood barrier in males was a cause⁽⁷⁾. Also, Al Odda et al.⁽⁷⁾ found a higher 3-year survival rate for patients afflicted with B-cell ALL (74.1%) than that of patients with T-cell ALL (64.3%), although this difference was huge in the current study (84.5% for B-cell ALL as compared to 50% for T-cell ALL).

However, our finding was nearer to Alecsa et al. ⁽¹²⁾, which found a 3-year survival rate of 78.9% for B-cell ALL compared to 64.9% for T-cell ALL.

In conclusion, the five-year survival rate was 80.9% in the current study. Further, the associations of the patient age groups, gender, WBC groups, risk groups, and post-induction status with the five year survival rates were insignificant. However, the frequency of some characteristics was more than the others. However, the association of the five-year survival rate with immunophenotyping was statistically significant (p-value = .014).

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The authors have nothing to declare.

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