



Mortality assessment of pediatric patients with acute lymphocytic leukemia in Southern Iran

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Abstract

Introduction: According to the statistics, cancer is now the second leading cause of disease-related death. Different cancers are more common among various age groups. Reportedly, leukemias are the most common pediatric cancer, and acute lymphoblastic leukemia (ALL) is known as the most prevalent cancer in children of this age.

Objectives: This study aims to determine the mortality rate of ALL in the pediatric age group admitted to Shafa Hospital in Khuzestan province, Iran.

Materials and Methods: The present descriptive epidemiological study was conducted on children and adolescents with ALL diagnoses in 2016 to 2019. In this regard, data on mortality caused by ALL in 98 patients was analyzed in a period of two years.

Results: Based on the findings, 98 patients comprised 60 boys and 40 girls. The most common age group was 2–10 years (71.4%), and pre-B ALL (81.6%) was the most prevalent ALL subtype. The mortality rate was 33% in 2016 and 8.8% in 2019. The highest mortality rate in terms of subtype was in the T-cell acute lymphoblastic leukemia (T-ALL) subgroup (41.6%), and the highest mortality rate based on the affected age group was in children over ten years (37.5%).

Conclusion: The five-year survival rate of ALL was 67% in 2016, and the three-year survival rate was 91.2% in 2019 in this region, mostly in males and in the age group of 2–10 years. Moreover, the survival rate was associated with the disease type and the diagnosis age.

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Introduction

Cancer has become one of the most serious life-threatening diseases today. According to the World Health Organization (WHO) and the American Cancer Society (ACS), the risk of cancer is 20.2% during the normal life of a 0-74-year-old person (1). The wide age range of this disease, which covers from birth to old age, justifies the need to pay attention to this disease in all age groups. In addition, the disease is completely age-dependent regarding the specific type of cancer involved, mortality rate, medication, treatment, and prognosis (1). Cancers range from low prognosis, such as pancreatic cancer with surgical treatment, to high prognosis, such as some pediatric leukemias with a treatment merely by chemotherapy. Pediatric cancer rarely occurs. Among cancers, acute leukemias-although relatively low in the general population are very sensitive due to their low survival rate and high incidence in children (2). The etiology of pediatric leukemia is unknown; it is probably a multifactorial disease since genetic and

Key point

This study aims to determine the mortality rate of acute lymphocytic leukemia in pediatric patients admitted to Shafa Hospital in Khuzestan province, Iran. This study analyzed 98 children and adolescents diagnosed with acute lymphocytic leukemia in Ahvaz between 2016 and 2019. The mortality rate was 33% in 2016 and 8.8% in 2019, with the highest mortality rate in the T-cell acute lymphoblastic leukemia subgroup and children over 10 years.

environmental factors play an important role in its malignant transformation (3). Acute lymphoblastic leukemia (ALL) is the most common childhood cancer, and it is more common in boys than in girls between the ages of two and five years old (4). The ALL-tumor forms from cells with progenitor lymphocytes or lymphoblasts. In leukemia, lymphocytes have uncontrolled activity, are incapable of providing a normal immune response, and do not produce healthy bone marrow cells, resulting in anemia, thrombocytopenia, and loss of white blood

cells that are not lymphocytes (particularly neutrophils or neutropenia) (5). Most cases are thought to occur due to chromosomal mutations in lymphoid cells after pregnancy. Exposure to diagnostic radiation in both intrauterine and fetal environments is associated with an increased incidence of ALL. In some developing countries, there is an association between precursor B-cell acute lymphoblastic leukemia (B-ALL) and the Epstein-Barr virus (3). The ALL classification is based on morphology, phenotype, and measurement of membrane surface markers, cytogenetics, and genetic studies. Approximately 85% of ALL cases are B-lymphoblastic leukemia. About 15% of T-lymphoblastic leukemia and about 1% of adult B cells are called Burkitt's leukemia (6). The initial symptoms of ALL are usually nonspecific and relatively brief. Anemia and thrombocytopenia are seen in most patients. Additionally, a cerebrospinal fluid (CSF) analysis is included in the initial examination. Evidence of central nervous system (CNS) involvement reflects the poorer stage of leukemia and the need for systemic and further CNS treatment (5). The prognosis for ALL has been steadily improving since the 1980s. The five-year event-free survival (EFS) rate for pediatric ALL is currently approaching 90% in developed countries. In addition, the overall five-year and 10-year survival rates have been reported to be 90% and 85-88%, respectively (7). Significant progress has been made in the last decade in treating and understanding the structure and biology of lymphocytic and myeloid leukemias in children and adults. Current therapies, from chemotherapy to stem cell transplantation and supportive care, help treat approximately 80% of newly diagnosed lymphoblastic leukemia children and 50% of patients with myeloid neoplasms (8).

Objectives

The purpose of this study is to determine the mortality rate of ALL in the pediatric age group admitted to Shafa Hospital in Khuzestan Province, Iran.

Materials and Methods

Study design

The present descriptive cross-sectional and retrospective epidemiological study was conducted on all pediatric patients with ALL who were diagnosed in 2016 and 2019 and admitted to Shafa Hospital of Ahvaz. Inclusion criteria were all patients with ALL confirmed by laboratory data, pathology, and a hematologist and oncologist examination. Exclusion criteria were individuals with incomplete registered information. Patient information, including age, gender, type of leukemia, ALL subtype, and five-year survival, was recorded according to hospital information.

Statistical analysis

SPSS 22 software was used to calculate and analyze the raw data statistically, and Excel software was used to draw the chart.

Results

The current study examined data related to ALL mortality in children referred in a two-year period. According to the findings, a total of 98 patients with ALL were included in the study, consisting of 59 boys (60%) and 39 girls (40%) (Figures 1-8).

Based on age, the patients were divided into three age groups; under 2 years, 2 to 10 years, and over 10 years, with 4 (4.08%) under 2 years, 70 (71.4%) between 2 and 10 years, and 24 (24.4%) over 10 years (Figure 2).

Based on the disease subtype, pre-B-ALL was present in 80 (81.6%), mature-ALL in 3 (3.06%), and T-cell-ALL in 12 (15.3%) (Figure 3).

Based on patient mortality, the total number of deceased patients was 22 (22.4%), of which 18 cases were in 2016 (33% of the total number of patients this year) and 4 cases in 2019 (8.8% of the total number of patients this year) (Figure 4).

Based on the sex ratio of mortality, out of 18 cases, 5 were girls (27%), and 13 were boys (73%) (Figure 5). Out of 4 cases, 2 were girls (50%) and 2 were boys in 2019 (Figure 6).

In terms of mortality and dispersion in age groups, one case (25%) had died out of a total of 4 cases with ALL in the age range of 0–2 years, 12 cases (17.1%) had died out of a total of 70 cases with ALL in the age range of 2–10 years, and 9 cases (37.5%) had died out of a total of 24 cases with ALL in the age group over 10 years.

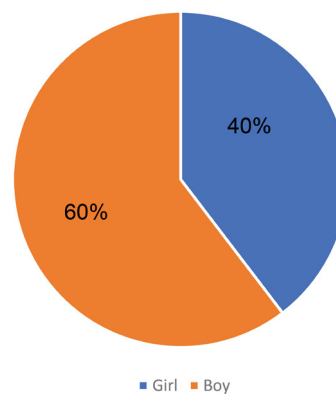


Figure 1. Frequency distribution of ALL in hospitalized patients based on gender.

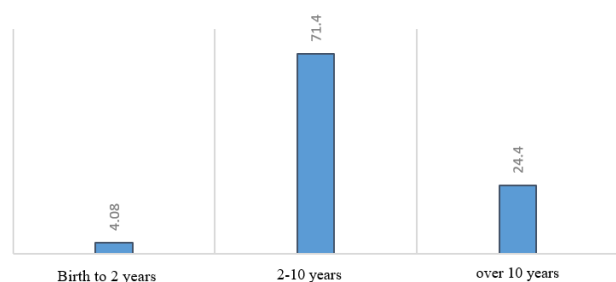


Figure 2. Frequency distribution of ALL in hospitalized patients based on age range of disease onset.

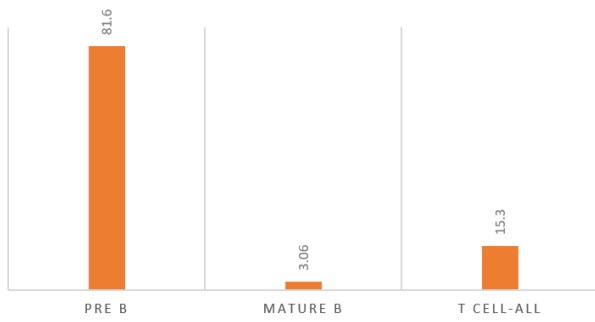


Figure 3. Frequency distribution of ALL subtypes in hospitalized patients.

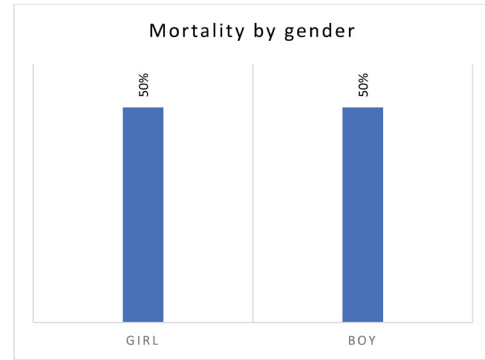


Figure 6. Frequency distribution of ALL mortality detected in 2019 based on gender

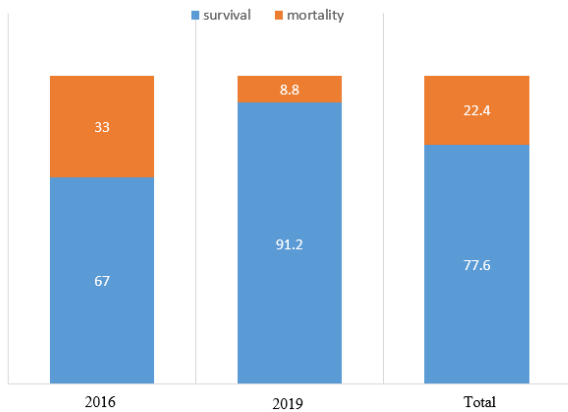


Figure 4. Frequency distribution of ALL mortality in diagnosed patients.

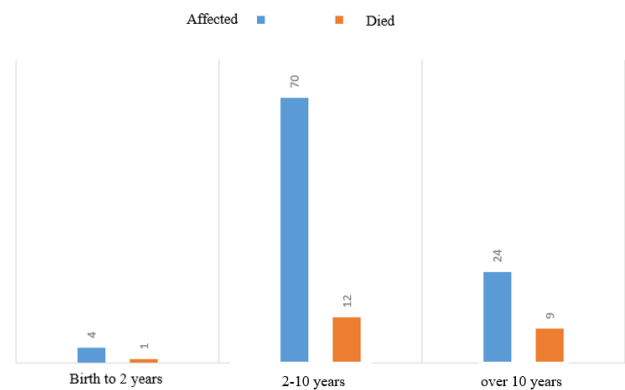


Figure 7. Frequency distribution of ALL deaths in the hospital based on age classification

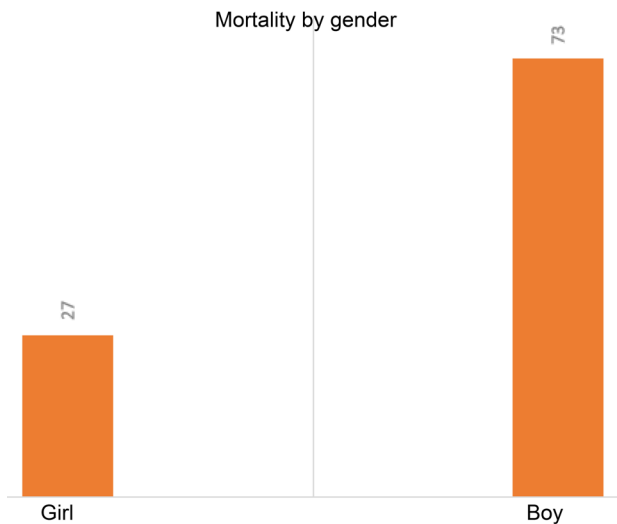


Figure 5. Frequency distribution of ALL mortality detected in 2016 based on gender.

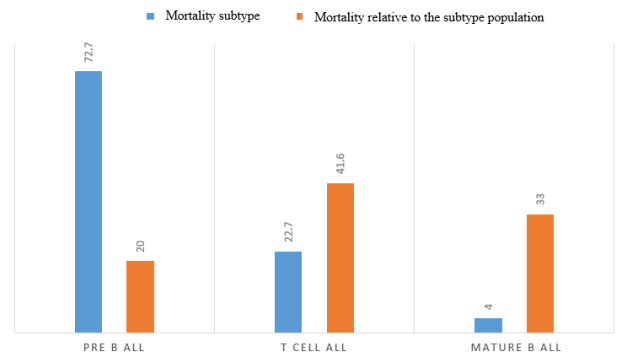


Figure 8. Frequency distribution of ALL mortality based on disease subtype in diagnosed patients

Based on patient mortality in terms of the disease subtype, out of 22 cases of mortality, 16 (72.7%) had pre-B-ALL, which is 80% of the total number of patients with this subtype, or 20% of the same population. Out of 22 mortality cases, 5 cases (22.7%) were T-cell-ALL, which was 41.6% compared to the subgroup population of 12 cases. Finally, one case of mature B cell-ALL mortality was

recorded, which was 4% of the total and 33% of the disease population.

Discussion

The present study aimed to evaluate the pediatric ALL mortality in the Shafa Hospital of Ahvaz in Iran, which was identified in 2016 and 2019. Of the 98 patients, 53 were registered in 2016 and 45 in 2019. Of the 53 ALL patients in 2016, 18 died (33%), and the five-year ALL survival was 66%, according to the study analysis. The number of

deaths was 4 in 2019, with an 8.8% mortality rate relative to 45 newly diagnosed patients this year and a three-year survival rate of 91.2%. In the present study, although the number of affected boys was higher (60% boys versus 40% girls), no significant difference was observed in the overall mortality rate of the two groups. Regarding age groups, the highest incidence rates were in the group of 2 to 10 years (71.4%), but the mortality rate was 17.1%, which was a lower percentage compared to the age group over 10 years. For the ALL subgroups, we examined three subgroups: pre-B cell ALL, T cell ALL, and mature B-cell ALL. The highest number of diagnoses was in pre-B-ALL; 81.6% of cases were diagnosed in this group, and the mortality rate was 20% compared to this group. The highest mortality rate in T-cell ALL was 41.6%. In a study by Varghese et al on 75 ALL patients, the five-year survival rate was more than 90% in developed countries but only 40% in India, and the event-free cases were 28% in this study. The reason for this condition was attributed to the poor nutritional status of these children at the time of diagnosis, their weight loss, poor quality of care compared to developed countries, and possibly differences in approach to disease (9). Moreover, in the study by Dreyer et al on 150 patients, children older than 10 years were in the high-risk prognosis group. Additionally, those over the age of 13 and those under one year old were at high risk (10). As compared with the total population, children over 10 years of age had a mortality rate of 37.5%. The second rank belonged to children under two years old (25%), which is not very helpful according to the general statistics of patients of this age. Regarding the immunophenotype of the disease, precursor T cell ALL and mature B cell ALL, in particular, are said to have a poor prognosis. In our study, out of the total number of cases diagnosed in these two subtypes, 11 were T cell-ALL, and only four patients were diagnosed with mature B-ALL, with a mortality rate of 41.6% for T cell-ALL and 33% for mature B-ALL relative to the population detected. In a review article, Raetz and Teachey noted that the T-ALL accounted for approximately 12–15% of all ALL cases diagnosed in pediatric patients, which is significant because of its unique clinical and biological characteristics. Based on history, the T-ALL outcomes were lower than B-ALL (11). According to preB-ALL statistics, the total number of patients was 80, which accounted for 72.7% of patients, and the mortality rate of this group was 20%. In studies, preB cell-ALL is examined by the genetic translocation type approach, which we did not examine in this study. Crist et al investigated various genetic translocations in ALL. Among these cases, the translocation t (12:21) with the highest incidence (25%) generally has a favorable prognosis and survival above 90%. The translocation t (9:22) in ALL with a poor prognosis has an incidence of about 4%. In addition, the translocation t (1:19) has a poor prognosis with an incidence of about 20% (12). The overall survival of preB-ALL is estimated at more than 80%, but the overall survival rate in this subtype has been around

80% in this study, which is lower than global statistics. In a retrospective study, de Lima et al examined pediatric ALL between 1958 and 2018 in Poland. This study was performed on 710 pediatric patients during these years. Five-year survival rate (pOS), event-free survival rate (pEFS), and risk of recurrence (pRR) have been reviewed and compared over the years. Over the past 60 years, the five-year survival rate has increased from 1.2% to 90.7%, the pEFS has increased from 1.2% to 86.6%, and the risk of recurrence has decreased from 9.9% to 98.8%. The mortality rate in patients undergoing chemotherapy and bone marrow transplantation had decreased to 9.9% during these sixty years; however, no significant survival superiority was observed between those with and without bone marrow transplantation (13). An analysis of mortality among Swedish children with ALL from 1988 to 2017 compared mortality with that for the general Swedish population. Based on 2397 Swedish pediatric patients with ALL from 1988 to 2017, this cohort study had an overall high standardized mortality ratio due to the significantly higher number of deaths than expected in the general population. A consistently high standardized mortality ratio was observed throughout this study in Swedish pediatric patients with ALL, similar to the survival evolution observed in the young general population (14).

Conclusion

Leukemia mortality in the Shafa Hospital of Ahvaz, a leukemia center in the Khuzestan province of Iran, is higher than the global statistics, which can be attributed to various reasons such as the type of translocations in the province, the nutritional status of children, the referral rate, the speed of diagnosis of primary cases in the medical system of the province, and the medical facilities of the province, which need further investigation and more detailed statistical analysis. Another influential issue is the developing situation in the country, which probably refers to the lack of facilities and the medical system, as well as the weak culture of timely doctor visits.

Suggestions

A comprehensive study of patients' translocations as well as the determination of refractory cases are suggested for future studies. In addition, we recommend training physicians and other specialists in the early symptoms of the disease, referring them to specialized cancer treatment centers more quickly, educating parents to become familiar with the symptoms and suspected cases, and encouraging them to visit a doctor. According to the results of studies on the impact of environmental factors on the risk of developing leukemia, it seems necessary to study the province's environment and control the environmental issues causing the disease.

Limitations of the study

The small sample of the patients and the single-center

study were the main limitations of the present study.

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Authors' contribution

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Supervision: Kaveh Jaseb.

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Ethical issues

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki. It was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (Ethical code#IR.AJUMS.HGOLESTAN.REC.1399.026). Before any intervention, all participants provided written informed consent. The study was extracted from Morteza Kabgani's general practitioner thesis in the department of pediatrics, school of medicine Ahvaz Jundishapur University of medical sciences (Thesis #U-330096449). The authors have fully complied with ethical issues, such as plagiarism, data fabrication, and double publication.

Conflicts of interest

The authors declare that they have no competing interests.

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