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Original Article

# Perspectives on Leukemia in Children under 15 Years of Age: Convergence of Clinical and Statistical Information in the Center of Iran

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## Abstract

**Background:** Leukemia is the most common childhood malignancy. Understanding its clinical manifestations and laboratory findings in different regions is essential for early detection and timely management. Despite limited exhaustive studies in central Iran, this study provides a comprehensive analysis of the clinical and laboratory data collected in Yazd Province over a ten-year period.

**Materials and Methods:** This retrospective descriptive study analyzed 378 children under 15 diagnosed with leukemia at Shahid Sadoughi Hospital between 2014 and 2023. Data included demographics, clinical symptoms, and blood counts. Statistical analysis was done using SPSS v20 with Chi-square and ANOVA tests, considering $P < 0.05$ as significant.

**Results:** This study included 213 males (56.6%) and 165 females (43.7%)(M: F =1.29:1), with a mean diagnostic age of 5.42 ± 3.85 years; 61.4% were ≤ 5 years old. Acute lymphoblastic leukemia (ALL) was the predominant subtype (89.7%). Fever (46%), bone pain (27.5%), and weakness/lethargy (26.2%) were the most common clinical manifestations. The subtype analysis revealed that ecchymosis and respiratory symptoms were significantly more frequent in patients with acute myeloid leukemia (AML) than in patients ALL (30.3% vs. 14.1%, P = 0.03; and 21.2% vs. 7.1%, P = 0.01, respectively), while weight loss was highest in chronic myelogenous leukemia (CML) (40%, P = 0.03). Hematologic abnormalities included anemia (85.4%), thrombocytopenia (59.2%), and hyper leukocytosis (17.2%). Median WBC was higher in CML (31 $mm^3$), whereas median lymphocyte percentages were higher in ALL (60 %). Males also had higher RBC counts (P = 0.039).

**Conclusion:** The findings confirm that ALL is the predominant leukemia in this population. The disease often presents with nonspecific systemic symptoms, highlighting the critical role of complete blood count as an essential screening tool for early diagnosis. Recognizing these patterns may support earlier referral, diagnosis, and initiation of appropriate treatment.

***Keywords:*** Children, Clinical manifestations, Epidemiology, Leukemia

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## Introduction

Childhood cancers represent a significant global public health challenge and account for a substantial proportion of mortality among children aged 0-14 years (1). The incidence rates of childhood cancers vary significantly across different countries, largely reflecting disparities in diagnostic capacity, the completeness of cancer registries, and access to healthcare systems (2). Despite the increasing incidence rates in developed countries, the mortality is declining there. In contrast, in low-income countries, the mortality from childhood cancers is rising due to inaccessible or severely limited diagnostic and therapeutic facilities, as well as delayed diagnosis (3, 4). In Iran, a meta-analysis estimated an incidence rate of approximately170 per million among children aged 0-14 years (5).

Among the various malignancies occurring during childhood, leukemia has the highest prevalence, accounting for approximately 30% of all the cases (6).

Leukemia is classified into four main types based on the affected cell lineage (lymphoid or myeloid) and the clinical course of the disease (acute or chronic). In pediatric populations, acute lymphoblastic leukemia (ALL) is the most common form, accounting for approximately 80% of the cases (7, 8).

The process of uncontrolled growth in the bone marrow disrupts the production of healthy blood cells, resulting in a weakened immune system and dysfunction of vital organs such as the liver, spleen, and central nervous system (1, 9).

In addition to its high prevalence, leukemia imposes a significant psychological, social, and economic burden on patients, their families, and the healthcare system. This burden arises from its aggressive nature and the necessity for long-term, costly treatments such as chemotherapy, radiotherapy, and, in some cases, bone marrow transplantation. Despite the significant advances in treatment protocols that have increased the five-year survival rate for certain types of leukemia to over 90%, challenges such as treatment resistance, disease relapse, and long-term side effects persist. Therefore, early diagnosis is essential for improving prognosis and reducing complications (10).

However, achieving an early diagnosis is often challenging because the initial symptoms, such as fever, weakness, and pallor, are non-specific and easily mistaken for common, benign childhood illnesses. This diagnostic delay can allow the disease to progress and may also diminish the opportunity to initiate effective treatment (11).

Numerous studies worldwide, including those conducted in Iran, have examined various aspects of childhood leukemia. Mehrvar et al. (2014) demonstrated that ALL is the most common type, accounting for 84.5% of the cases, with a peak incidence between the ages of 2 and 5 years. They also found that fever and weakness are the most frequent initial symptoms (12).

Similarly, the results of the research by Shahverdi et al. (2020) indicated that fever (66.8%), pallor (52.3%), and bone pain (45%) were the most common symptoms (13). At an international level, Clarke et al. (2016) emphasized that a combination of non-specific symptoms should be considered a major warning sign, warranting the immediate referral of patients for further investigation (13, 14).

Despite numerous valuable studies, significant research gaps remain in understanding the regional distribution of the disease in Iran. Most prior studies have either focused on the specific aspects of the disease or been conducted over relatively short time periods. The novelty of this study lies not only in the comprehensive analysis of the demographic, clinical, and laboratory data collected in Yazd Province over a ten-year period (2014-2023) but also in highlighting the critical need to reassess and update epidemiological investigations of childhood cancer. Such efforts are essential to develop evidence-based strategies for prevention, diagnosis, and treatment. Moreover, Yazd Province, due to its central geographic location, industrial profile, and role as a migratory hub, serves as an ideal representative setting for examining disease patterns within heterogeneous populations. By providing an integrated overview of patient characteristics at diagnosis, this study aims to identify the key signs and symptoms that may serve as initial screening and diagnostic indicators. Therefore, the primary objective of this

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study is to delineate and analyze the epidemiological profile, clinical presentations, and laboratory findings of children under 15 years of age diagnosed with leukemia who have referred to a specialized hospital in Yazd.

## Material and Methods

This research is a descriptive cross-sectional study with a retrospective approach, designed to investigate and analyze the epidemiological, clinical, and laboratory characteristics of children with leukemia. The study was conducted from October 2024 to May 2025 after obtaining approval from the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, under the ethics code IR.SSU.MEDICINE.REC.1403.014. The research population included all the children under 15 years of age diagnosed with various types of leukemia, whose definitive diagnoses were registered at Shahid Sadoughi Hospital in Yazd, the main referral center for pediatric oncology patients in the province and the neighboring regions from the beginning of 2014 to the end of 2023.

Sampling in this study was conducted using the census method, meaning that all the patients who met the inclusion criteria during the specified time period were examined. The inclusion criteria were age less than 15 years at diagnosis, a definitive diagnosis of one of the leukemia types, namely ALL, AML or CML based on pathology reports, and availability of complete and accessible medical records containing demographic and clinical information as well as the results from the initial complete blood count (CBC) test. The exclusion criteria included incomplete records lacking key demographic, clinical, or laboratory data, a final diagnosis other than leukemia, and records that were inaccessible due to improper archiving. To ensure data integrity, all the records missing essential information were excluded from the analysis. The data extraction was performed by two independent researchers using a standardized checklist, and a random 10% of records were rechecked for accuracy. Any identified discrepancies were resolved by consensus.

In total, of the 397 initially identified records, 19 were excluded due to missing key information. Ultimately, the data from 378 patients were included in the analysis. The required data, including age, gender, place of residence, first clinical manifestation, most common clinical symptoms, first laboratory findings, and type of leukemia were extracted from the patients' medical records.

The data were collected in three sections. The first section focused on patient demographic information and included variables such as age, gender, and place of residence. The second section addressed the type of leukemia, the initial clinical symptoms, and the most common clinical manifestations. The third section detailed the patients' initial complete blood count (CBC) test results, including quantitative values of white blood cells (WBC), red blood cells (RBC), hemoglobin (Hb), hematocrit (Hct), platelets (PLT), neutrophils, and lymphocytes.

In this study, anemia was defined according to WHO pediatric thresholds, which vary by age and gender (e.g., hemoglobin < 12 g/dL for children under 15 years). Thrombocytopenia was defined as a platelet count below 150,000/µL (15).

### *Statistical analysis*

The data were analyzed using the SPSS software, version 20. According to the type of data distribution, both parametric and non-parametric tests were employed. The normality of the quantitative variables was assessed with the Kolmogorov-Smirnov test. For the parametric tests, the mean and standard deviation values were reported. For non-parametric tests, medians and interquartile ranges were reported. The qualitative variables were presented as frequencies and percentages. To compare the means of the quantitative variables between two groups of patients, independent t-test or Mann-Whitney U test was used. For more than two groups, one-way analysis of variance (ANOVA) or the Kruskal-Wallis test was applied. Moreover, the Chi-square test was used to compare the qualitative variables. The significance level for all the tests was considered to be 0.05.

## Results

In this study, the data from 378 children

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under15 years of age with leukemia admitted at Shahid Sadoughi Hospital in Yazd over a ten-year period (2014-2023) were analyzed. The examination of the demographic characteristics showed that, of all the patients, 213 (56.6%) were boys and 165 (43.7%) were girls, indicating a boy-to-girl ratio of 1.29 to 1. The average age of the patients was 5.42 ± 3.85 years, and their highest frequency was in the 0-to-5 years age group (61.4%), followed by the 5-to-10 years (23.5%) and 10-to-15 years (15.1%) age groups. In terms of residence, a total of 140 patients (37%) were inhabitants of Yazd City, 121 (32%) resided in various counties within Yazd Province, and 117 (31%) were referred from other neighboring provinces. The predominant form of leukemia was ALL in 339 cases (89.7%), followed by AML in 33 cases (8.9%) and CML in five cases (1.3%). The statistical analysis of the association between the demographic variables and the leukemia type showed that age, gender, and place of residence did not differ significantly among the different leukemia groups (P > 0.05). The details of these findings are presented in Table I.

Examining the clinical manifestations at presentation showed that fever, with a frequency of 46%, was the most common clinical manifestation overall. Following that were bone pain (27.5%), weakness and lethargy (26.2%), hepatosplenomegaly (16.7%), pallor (16.1%), and gastrointestinal symptoms (15.6%). In a comparative analysis of the leukemia types, although most symptoms showed no significant difference, ecchymosis (bruising) was significantly more common in the AML patients (30.3%) than in the ALL patients (14.1%) (P = 0.03). Also, respiratory symptoms were more prevalent in the AML group (21.2%) than in the ALL group (7.1%), and this difference was also statistically significant (P = 0.01). Weight loss was reported in the CML (40%), AML (6.1%), and ALL (8.2%) patients too, and the difference was significant (P = 0.03). Further details are provided in Table II.

Regarding the first reported symptom that led the patient to seek medical attention, fever (31.2% in ALL and 39.4% in AML) remained the most common. Next to that, weakness and lethargy (15.0%) and bone pain (11.8%) in ALL were the most important initial symptoms. No significant difference was observed in the distribution of the first symptoms among the different leukemia groups (P = 0.65). The other initial symptoms recorded based on leukemia type are presented in Table III.

Table IV summarizes the hematological characteristics of the patients across different leukemia subtypes. The mean hemoglobin level among the patients was 9.09 ± 2.68 g/dL, and anemia (Hb < 12 g/dL) was observed in 85.4% of the children. Thrombocytopenia (PLT < 150,000/µL) was present in 59.2% of the patients. The WBC counts demonstrated substantial variability; 20.6% of the patients had leukopenia (WBC < 4,000/µL), 32.3% had leukocytosis (WBC > 10,000/µL), and approximately 30% had WBC counts within the normal range. Among them, 17.2% exhibited hyperleukocytosis (WBC > 50,000/µL)( Table V). The one-way ANOVA comparing the mean hematological indices across the leukemia subgroups revealed no statistically significant differences in mean red blood cell count, hemoglobin level, and hematocrit (P > 0.05).

Given the non-normal distribution of the data, the WBC count, platelet count, neutrophil percentage, and lymphocyte percentage were expressed as medians (interquartile range). The median WBC count was significantly higher in the CML group, as compared to ALL and AML (P = 0.003). Although platelet counts was higher in CML, the difference was not statistically significant (P = 0.37). A significant difference in neutrophil percentages was observed among the leukemia subgroups, with CML showing the highest median values (P = 0.02). Conversely, lymphocyte percentages were significantly higher in ALL and lowest in CML (P = 0.01). No significant difference in monocyte percentages was observed among the three groups (P = 0.54).

Table VI presents the association between gender and CBC parameters. An independent two-sample t-test revealed a statistically significant difference in red blood cell (RBC) count (P = 0.039), with a higher mean value in males (3.46 ± 0.97) than in females (3.25 ± 1.00). However, no statistically significant differences were observed between the genders in terms of the hemoglobin level, hematocrit, white blood cell count, or platelet

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count (all P > 0.05).

Furthermore, as the evidence showed, 130 patients (38.2%) had two clinical symptoms, 85 (25%) had only one symptom, 84 (24.7%) experienced three symptoms, and only 41 patients (12.1%) reported more than four clinical symptoms simultaneously. Based on the frequency of incidence and patient referrals, the highest number of cases was reported in 2014 (n = 58, 15.2%), followed by 2019 (n = 46, 12.2%) and 2022 (n = 42, 11.1%) (Figure 1).

*Table I. Frequency of children with different types of leukemia by age, gender, and place of residence*

| Type of leukemia | Age (year) n(%) | | | *P-value | Gender n (%) | | *P-value | Residence n (%) | | | *P-value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0-5 | 5-10 | 10-15 | | Male | Female | | Yazd | Cities of Yazd Province | Other Cities | |
| ALL | 211 (61.9) | 78 (22.9) | 51 (15.0) | 0.83 | 193 (56.8) | 147 (43.2) | 0.73 | 126 (37.1) | 108 (31.8) | 106 (31.2) | 0.39 |
| AML | 20 (60.6) | 9 (27.3) | 4 (12.1) | | 18 (54.5) | 15 (45.5) | | 14 (42.4) | 11 (33.3) | 8 (24.2) | |
| CML | 2 (40.0) | 2 (40.0) | 1 (20.0) | | 2 (40.0) | 3 (60.0) | | 0 (0.0) | 2 (40.0) | 3 (60.0) | |

* Chi-square test

*Table II. Frequency of children with different types of leukemia based on the most common clinical manifestations*

| Clinical manifestation | Acute lymphoblastic leukemia n (%) | Acute myeloid leukemia n (%) | Chronic myeloid leukemia n (%) | *P-value |
|---|---|---|---|---|
| **Fever** | 151 (44.4) | 20 (60.6) | 3 (60.0) | 0.16 |
| **Sweating** | 23 (6.8) | 1 (3.0) | 0 (0.0) | 0.59 |
| **Weakness/fatigue** | 89 (26.2) | 9 (27.3) | 1 (20.0) | 0.94 |
| **Hepatosplenomegaly** | 60 (17.6) | 1 (3.0) | 2 (40.0) | 0.15 |
| **Bone pain** | 93 (27.4) | 9 (27.3) | 2 (40.0) | 0.82 |
| **Weight loss** | 28 (8.2) | 2 (6.1) | 2 (40.0) | 0.03 |
| **Anorexia** | 44 (12.9) | 1 (3.0) | 1 (20.0) | 0.21 |
| **Epistaxis** | 13 (3.8) | 2 (6.1) | 0 (0.0) | 0.73 |
| **Ecchymosis** | 48 (14.1) | 10 (30.3) | 0 (0.0) | 0.03 |
| **Edema** | 34 (10.0) | 3 (9.1) | 1 (20.0) | 0.74 |
| **Gastrointestinal** | 56 (16.5) | 2 (6.1) | 1 (20.0) | 0.28 |
| **Respiratory** | 24 (7.1) | 7 (21.2) | 0 (0.0) | 0.01 |
| **Pallor** | 59 (17.4) | 2 (6.1) | 0 (0.0) | 0.14 |
| **Anemia** | 3 (0.9) | 0 (0.0) | 0 (0.0) | 0.84 |

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| | | | | |
|---|---|---|---|---|
| **Lymphadenopathy** | 41 (12.1) | 4 (12.1) | 0 (0.0) | 0.71 |
| **Common cold** | 45 (13.2) | 4 (12.1) | 0 (0.0) | 0.67 |
| **Leukopenia** | 3 (0.9) | 0 (0.0) | 0 (0.0) | 0.84 |
| **Other** | 83 (24.4) | 10 (30.3) | 0 (0.0) | 0.33 |

*Chi-square test

*Table III: The other initial symptoms recorded based on leukemia type*

| First symptom | Acute lymphoblastic leukemia n (%) | Acute myeloid leukemia n (%) | Chronic myeloid leukemia n (%) | *P-value |
|---|---|---|---|---|
| **Fever** | 106 (31.2) | 13 (39.4) | 1 (20.0) | 0.65 |
| **Weakness** | 51 (15.0) | 5 (15.2) | 1 (20.0) | |
| **Pallor** | 23 (6.8) | 1 (3.0) | 0 (0.0) | |
| **Epistaxis** | 9 (2.6) | 1 (3.0) | 0 (0.0) | |
| **Bone pain** | 40 (11.8) | 2 (6.1) | 1 (20.0) | |
| **Edema** | 29 (8.5) | 2 (6.1) | 0 (0.0) | |
| **Gastrointestinal symptoms** | 36 (10.6) | 1 (3.0) | 2 (40.0) | |
| **Ecchymosis** | 24 (7.1) | 4 (12.1) | 0 (0.0) | |
| **Icterus & jaundice** | 5 (1.5) | 2 (6.1) | 0 (0.0) | |
| **Other** | 17 (5.0) | 2 (6.1) | 0 (0.0) | |

*Chi-square test

*Table IV. Hematological characteristics and distribution of CBC parameters in pediatric leukemia patients*

| Parameter | Acute lymphoblastic leukemia (Mean ± SD)/ Median ($Q_1$-Q3) | Acute myeloid leukemia (Mean ± SD)/ Median ($Q_1$-Q3) | Chronic myeloid leukemia (Mean ± SD)/ Median ($Q_1$-Q3) | P-value |
|---|---|---|---|---|
| RBC | 3.39 ± 0.99 | 3.11 ± 1.00 | 3.47 ± 0.65 | 0.27 |
| WBC | 9/10 (4/62- 22/57) | 14/10 (7/15-31/05) | 31/0 (22/70- 31/00) | 0.003 |
| Hemoglobin | 9.09 ± 2.63 | 8.79 ± 2.87 | 8.64 ± 1.44 | 0.76 |
| Hematocrit | 27.82 ± 7.62 | 26.79 ± 8.40 | 26.16 ± 5.19 | 0.68 |
| Platelet | 98/00 (37/00- 271/25) | 71/0 (23/00- 240/00) | 111/0 (61/0- 463/0) | 0.37 |
| Neutrophil | 20/15 (10/00- 46/00) | 36/0 (12/50- 52/50) | 54/0 (40/50- 69/0) | 0.02 |
| Lymphocyte | 60/00 (32/00 – 83/00) | 51/60 (32/70- 65/70) | 16/0 (6/50- 42/0) | 0.01 |
| Monocyte | 0 (0/0- 3/0) | 1/0 (0/0- 3/00) | 0/0 (0/0- 3/00) | 0.54 |

* ANOVA test, ** Kruskal-Wallis test

*Table V. Frequency distribution of WBC, hemoglobin and platelet levels in children with leukemia*

| Variable | Category | n (%) |
|---|---|---|
| White blood cells (WBC) **$mm^3$** | < 4000 | 78 (20.6) |
| | 4000-10000 | 113 (29.9) |
| | 10000-50000 | 122 (32.0) |
| | > 50000/ | 65 (17.2) |
| Hemoglobin **g/dL** | < 8 | 132 (34.9) |
| | 8-12 | 191 (50.5) |
| | > 12 | 55 (14.6) |
| Platelet **$mm^3$** | < 50000 | 123 (32.5) |
| | 50000-100000 | 71 (18.8) |
| | 100000-150000 | 30 (7.9) |
| | > 150000 | 154 (40.7) |

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*Table VI. Association between gender and CBC parameters*

| Parameter | Gender | Mean ± SD / Median (Q1–Q3) | P-value |
|---|---|---|---|
| Red blood cells (RBC) | Male | 3.46 ± 0.97 | 0.039* |
| | Female | 3.25 ± 1.00 | |
| Hemoglobin | Male | 9.26 ± 2.66 | 0.087* |
| | Female | 8.80 ± 2.58 | |
| Hematocrit | Male | 28.15 ± 7.53 | 0.205* |
| | Female | 27.14 ± 7.80 | |
| White blood cells (WBC) | Male | 9.10 (4.50–25.55) | 0.569** |
| | Female | 10.30 (5.15–25.35) | |
| Platelet count | Male | 99.00 (37.00–287.50) | 0.353** |
| | Female | 90.00 (36.50–243.00) | |

* Independent two-sample t-test, ** Mann-Whitney test

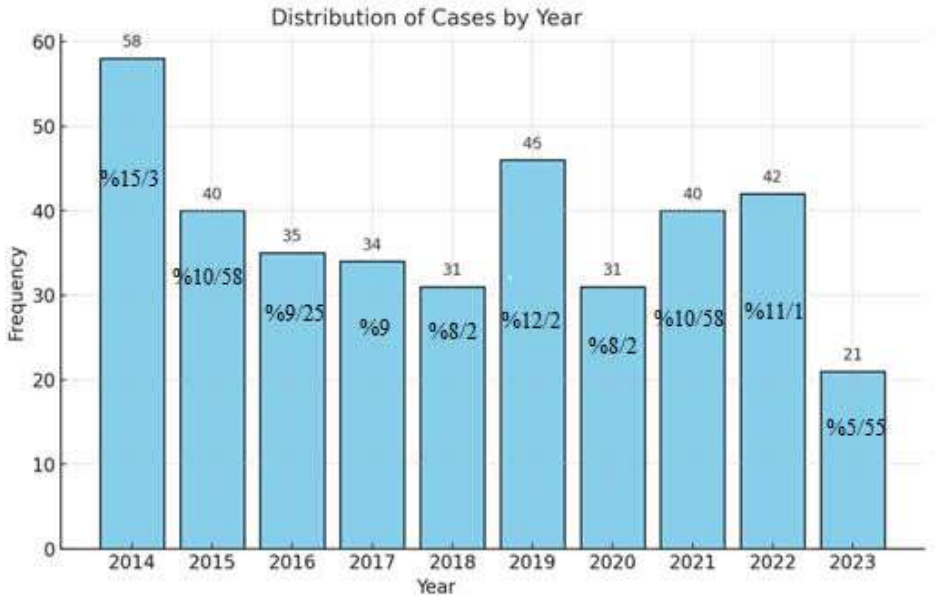


Figure 1. Annual distribution of pediatric leukemia cases from 2014 to 2023

## Discussion

This study aimed to provide a comprehensive overview of the epidemiological, clinical, and laboratory characteristics of childhood leukemia in central Iran over a ten-year period. While confirming many globally recognized patterns, the findings reveal important details about the studied population, early diagnosis and various aspects of leukemia. These insights will guide future diagnostic, clinical, and research efforts.

One of the key findings of this study was the higher prevalence of ALL than AML. This aligns closely with global statistics and numerous domestic studies, having identified ALL as the predominant form of childhood leukemia (5, 15). The consistent pattern observed across diverse geographical regions and ethnicities suggests an inherent biological predisposition within the lymphoid cell lineage during early life. It also supports the hypothesis of immune system vulnerability during early life, which is corroborated by the findings of Mehrvar et al. (12) and Biswas et al. (16). Rapid immune system development and high rates of cell division are the characteristics of this age period, making cells more vulnerable to genetic errors and external factors (17).

Another finding was the higher prevalence of leukemia in boys, with a ratio of 1.29 to 1. This gender predominance is a well-documented phenomenon in the epidemiology of childhood leukemia and is observed in most large studies, including reports from cancer registries in America and Europe (10, 18, 19). The reasons for this

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gender difference are not fully understood, but hypotheses include the effects of gender hormones on lymphoid cell proliferation and genetic differences related to the X chromosome in immune response and tumor control (20). The lack of a statistically significant association between gender and leukemia type in our study indicates that this male predominance probably exists in both main types of leukemia (ALL and AML) and that the biological factors associated with gender influence the overall risk, rather than the subtype-specific risk.

Among the clinical manifestations, fever, bone pain, and weakness and fatigue were the most common. These findings are consistent with the results obtained by Shahverdi et al. (13), who reported fever and pallor as the most prominent symptoms as well as Hunger and Mullighan (7) who highlighted the significance of bone and joint pain as a misleading symptom. Fever is caused by the release of inflammatory cytokines through cancerous cells or neutropenia in patients with leukemia, which increases their susceptibility to infections. Bone pain is also the result of leukemic cell proliferation infiltration and pressure in the bone marrow space. The nonspecific nature of these symptoms can lead to delayed diagnosis and can be easily mistaken for viral infections or musculoskeletal growth pains.

A significant finding of this study was the higher prevalence of ecchymosis and respiratory symptoms in patients with AML. The higher incidence of ecchymosis (bruising) in AML could be linked to more severe thrombocytopenia or platelet malfunction in this type of leukemia (21). Respiratory symptoms may also result from deeper neutropenia and opportunistic pulmonary infections or, in rare instances, from pulmonary infiltration by myeloid blasts (granulocytic sarcoma) (22). These findings underscore the need for heightened clinical vigilance when such symptoms are present, as they may indicate aggressive disease requiring urgent supportive care (23).

The laboratory findings of the present study highlight anemia and thrombocytopenia as the most prevalent hematologic abnormalities, reflecting malignant cell infiltration and bone marrow failure. These abnormalities are directly associated with clinical manifestations such as pallor, weakness, bleeding, and bruising. The results are consistent with the findings of Behnam et al. (24) and other studies conducted in this field; they underscore the role of the complete blood count (CBC) as the first and most essential initial diagnostic tool in children suspected of having leukemia (7).

In this study, the white blood cell count (WBC) was in a wide range from leukopenia to hyper leukocytosis. This high variability is a classic feature of acute leukemia. Approximately one-third of patients present low WBC, and nearly 17% have hyper leukocytosis (WBC > 50,000), which is itself considered an unfavorable prognostic factor requiring urgent management to prevent leukostasis (25). Significant differences in the mean neutrophil and lymphocyte counts were also noted between the two groups. Relative lymphocytosis in patients with ALL and relative neutrophilia in patients with CML are entirely consistent with the pathophysiological nature of these diseases and can be used as an initial diagnostic clue in CBC analysis. These findings were confirmed in the studies by Ibadullayeva et al. (26) and Goel et al. (27).

Regarding the association between gender and CBC parameters, a significant difference was observed only in red blood cell (RBC) count, while there was no significant difference between the two genders in the other blood parameters. This finding may reflect gender-related physiological differences in erythropoiesis, partly influenced by hormonal factors; however, in children with leukemia, these effects are likely attenuated by disease-related bone marrow involvement and treatment effects. The absence of significant gender differences in other CBC indices suggests that leukemic pathology and systemic factors play a more dominant role than biological gender in determining hematological profiles These findings are consistent with the previous research conducted in this field (28).

Another finding of this study was the fluctuations in the number of patient admissions across different years. Although a causal relationship cannot be inferred, these variations

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may reflect changes in referral patterns, demographic shifts, or alterations in access to healthcare services. Similar temporal fluctuations have been reported in studies on the incidence of childhood leukemia, which, in some cases, are associated with environmental factors or seasonal infections (29). For example, one reason for the decline in the reported cases in 2020 may partially be the disruptions in healthcare services during the COVID-19 pandemic. Delays in hospital admissions, reduced diagnostic efforts, and interruptions in referral systems have been documented in several studies during this period. These factors may have contributed to the underdiagnosis or delayed diagnosis of childhood malignancies, including leukemia (30). Also, the limited number of referrals in 2023 may be attributed to the incomplete capture of patient records and electronic data at the time of sample collection.

Further research focusing on regional referral systems and environmental determinants may help to elucidate the trends observed in this study.

## Conclusion

This 10-year retrospective study provides a comprehensive epidemiological, clinical, and laboratory profile of childhood leukemia in central Iran. The findings confirm that ALL is the predominant subtype, particularly among children under five years of age, with a higher prevalence in males. The most common presenting symptoms, i.e., fever, bone pain, weakness, and pallor, are nonspecific and can easily be mistaken for benign childhood illnesses, highlighting the risk of delayed diagnosis. Laboratory findings, especially anemia and thrombocytopenia, emphasize the critical role of the complete blood count (CBC) as the most accessible and cost-effective screening tool in resource-limited settings. Significant differences in WBC, neutrophil, and lymphocyte counts among leukemia subtypes provide additional diagnostic clues that may support earlier detection.

Beyond confirming global epidemiological patterns, this study offers region-specific insights into clinical presentations and laboratory variability. These findings may assist healthcare providers in improving early recognition, timely referral, and supportive care strategies. They also offer clear information to families regarding the warning signs of the disease, thus facilitating earlier medical consultation and intervention.

## Strengths and limitations

A notable advantage of this study is the development of a valuable database within a large and specific population, namely Yazd Province and the surrounding areas, thereby aiding the completion of the country's epidemiological map for childhood cancers. The study addresses a gap in comprehensive and long-term research by focusing on the provincial level, whereas many prior studies have been centered in major cities or covered shorter time spans. Consequently, a ten-year outlook from a regional treatment center facilitates a deeper understanding of the challenges and healthcare requirements beyond the capital. It can serve as a basis for more effective clinical interventions and future research in the battle against childhood cancer in Iran.

The present study was conducted at a single treatment center, so its results may not be fully generalizable to all parts of the country. Additionally, the lack of access to cytogenetic and molecular data did not allow for more precise patient classification and prognostic analyses. Despite these limitations, additional research is advised to concentrate on cytogenetic and molecular analyses, with the goal of more accurately classifying different leukemia subtypes and assessing their relationship with prognosis and treatment outcomes within the country's population. Conducting prospective and multi-center studies at a national level in Iran could offer a more detailed and accurate understanding of childhood leukemia epidemiology, risk factors, and treatment outcomes. The healthcare system can improve care quality by expanding its infrastructure, particularly through establishing a fully functioning referral system and offering support services for patients' relatives, taking into

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account the crucial role of the provided facilities in treating individuals from the province and the surrounding areas.

## Availability of Data

Available upon reasonable request from the authors.

## Ethical Considerations

The Ethics Committee of Shahid Sadoughi University of Medical Sciences approved the study (IR.SSU.MEDICINE.REC.1403.014).

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## Authors' Contributions

SHR and HN did the conceptualization and design of the study. NA contributed to the data collection. SHR, KHN and HN prepared the first draft of the manuscript. SN and NA critically revised and closely checked the proposal, the analysis and interpretation of the data and the design of the article. All the authors read and approved the final manuscript.

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## Conflict of Interest

The authors declare that they have no conflicts of interest.

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