

Research Article

Clinical Presentations of Acute Leukemia in Children's Cancer Units at Al-Kuwait Hospital, Sana'a City: A Cross-Sectional Study

Abdulrahman M Alhadi¹, Abdulrahman A Ishaq² and Hassan A Al-Shamahy^{2,3*}

¹Department of Pediatrics, Faculty of Medicine and Health Sciences, Sana'a University, Sana'a, Republic of Yemen

²Medical Microbiology and Clinical Immunology Department, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen

³Medical Microbiology Department, Faculty of Medicine, Genius University for Sciences & Technology, Dhamar city, Republic of Yemen

*Corresponding author: Prof. Hassan A Al-Shamahy, Faculty of Medicine and Health Sciences, Sana'a University, Genius University for Sciences and Technology, Dhamar/Sana'a, Yemen

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Abstract

Background and aims: Leukemia is a heterogeneous group of blood disorders consisting of several diverse and biologically distinct subgroups. Leukemia is the eleventh and tenth most common cause of cancer morbidity and mortality worldwide, respectively. There are insufficient data on clinical symptoms of acute leukemia in Yemen, particularly in the study area. Therefore, this cross-sectional study aimed to determine the clinical form of acute leukemia among children with leukemia in pediatric cancer units of Kuwait Hospital, Sana'a City.

Patients and method: A cross-sectional study was conducted on children with leukemia who were selectively treated in pediatric leukemia units at Kuwait Hospital in Sana'a. The mass diagnosis and histopathological prognosis in line with the French, American and British classifications of pediatric leukemia were formed in pediatric leukemia units, over a period of 7 years from 1 January 2015 to 31 December 2021. Factors associated with leukemia such as age, sex, clinical symptoms and outcome were studied.

Results: The mean \pm SD age of all cases was 7.96 ± 3.93 years. Most of the cases were in the age group 6-10 years (67.8%), followed by the age group 11-15 years (25.1%). As for gender, slightly more of the cases were males (53.3%), VS 46.7% in females (ratio=1.14-1). The cure rate was 40.56% while the death rate was 20 cases (6.19%). The relapse rate was 2.2%. The rest of the cases were in maintenance therapy (31.6%), induction therapy (15.2%), and consolidation (post-remission therapy) for 4.33% of cases. Most cases were ALL (83.3%) while AML was only 16.7%. The most common symptom was fever (78.3%), followed by pallor (34.4%), bleeding disorders (31.9%), and abdominal pain/distention (26.9%). Hepatomegaly was recorded in 5.6%, splenomegaly in 12.1%, lymphadenopathy in 10.8%, and 18.6% of the total patients had enlargement of all three organs.

Conclusion: ALL is the most common type of leukemia. The male-to-female ratio is roughly equal, and young children between the ages of 6-10 are most affected by leukemia. More comprehensive investigations of relevant factors and predictors using more recent diagnostic methods and investigation of association factors with valuation of the treatment protocols currently in use are needed.

Keywords: Childhood leukemia, Clinical presentation, Acute leukemia, Children, Sana'a City, Yemen

Introduction

Acute leukemia (ALs) are one of the most common types of cancer with approximately 20,000 cancers diagnosed and more than 10,000 deaths annually in the United States [1]. Acute leukemia represents tumors of hematopoietic cell precursors that manifest as clonal expansion of myeloid and lymphoid hematopoiesis [2]. Acute leukemia can be broadly categorized into acute lymphocytic leukemia and acute myeloid leukemia depending on the type of cell line affected. Hematopoietic tissue in the bone marrow is characterized by an overproduction of immature lymphocytes (a type of white blood cell). Acute lymphoblastic leukemia (ALL) occurs at all ages, from birth to puberty, but the incidence peaks between 2 and 6 years of age [3,4]. Acute Lymphocytic Leukemia (ALL) is clinically and morphologically heterogeneous. Morphologically, it is classified according to FAB

(French, American and British) criteria into L-1, L-2 and L-3 subtypes, which is clinically reproducible. Acute Myelogenous Leukemia (AML) refers to a group of hematological malignancies that arise within bone marrow precursors of myeloid, monocyte, erythroid and megakaryotic cell lineages. FAB classification system divides Acute Myelogenous Leukemia into M-0 to M-7 sub-types [5]. Improvements in treatment resulted in marked gains in survival, estimated at 79 percent at 5 years. The AML score was poorer than for ALL, with a 5-year survival rate of 41 percent [3,4]. The precise cause of leukemia is not up till now obvious. Nevertheless a lot of factors, mainly genetics, genetic mutations, epigenetic lesions, ionizing radiation, other chemical and occupational contacts, curative drugs, smoking and some viral agents, have been concerned in the development of leukemia [5-13]. In developing countries, the impact of leukemia is

attributed to premature death of children, loss of parents, failure of productivity due to disability, and prohibitive medical costs affecting the social, economic and health well-being of the population [14-16]. While leukemia is treated very well in the developed world, there is little evidence for the current status of the disease in Yemen in general and in the study area in particular. On the other hand, in Yemen as in most Arab countries, there are few specialized epidemiological registries dedicated to this field, which is why it is important to encourage, update, build and continue to provide studies on pediatric leukemia. The goal is to have a greater impact on public health, with early diagnosis and appropriate treatment aimed at enhancing survival and minimizing potential consequences. According to the limited Yemeni cancer studies, the most common types of cancers among Yemeni children and adults are leukemia (33.1%), lymphoma (31.5%), central nervous system tumors (7.2%), and bone tumors (5.2%) [17-22], while there are new published reports indicating an increased interest in communicable and non-communicable diseases that are closely linked to war, poverty, and the collapse of health systems in Yemen [23-30]. But there is insufficient data on the clinical symptoms of acute leukemia in Yemen, especially in the study area, so this cross-sectional study aimed to determine the clinical form of acute leukemia among children.

Patients and Method

A cross-sectional study was conducted on children with leukemia who were selectively treated in pediatric leukemia units at Kuwait Hospital, Sana'a. The mass diagnosis and histopathological diagnosis was formed in line with the French, American and British classifications of pediatric leukemia, over a period of 7 years from 1 January 2015 to 31 December 2021. Incidence-related factors were studied including ages, sex, clinical symptoms and outcomes.

Statistical Analysis

By using EPI Info statistical program version 6 (CDC, Atlanta, USA) the analysis of data was performed. Expressing the quantitative data as mean values, standard deviation (SD), when the data was normally distributed. Expressing the qualitative data as percentages; Chi square test was used for comparison of two variables to determine the *P* value.

Ethical Approval

Ethical approval was obtained from the Medical Research & Ethics Committee of the Faculty of Medicine and Health Sciences, Sana'a University. All data, including patient identification were kept confidential.

Results

The mean \pm SD age of all cases was 7.96 ± 3.93 years. Most of the cases were in the age group 6-10 years (67.8%), followed by the age group 11-15 years (25.1%), while only 7.1% of the cases were in the age group 1-5 years. As for gender, slightly more of the cases were males (53.3%), while the percentage of females was 46.7% (male to female ratio=1.14-1). Most of the patients were from rural areas counting 68.7% while only 31.3% were from urban areas (Table 1). The cure rate was 40.56% while the death rate was 20 cases (6.19%);

the relapse rate was 2.2%. The rest of the cases were in maintenance therapy (31.6%), induction therapy (15.2%), and consolidation (post-remission therapy) for 4.33% of cases (Table 2). Table 3 shows the prevalence of leukemia type among children with childhood leukemia in Sana'a, Yemen, and most cases were ALL (83.3%) while AML was only 16.7%. Table 4 shows the prevalence of clinical symptoms at the first visit among 323 children suffering from childhood leukemia. The most common symptom was fever counting 78.3%, followed by pallor (34.4%), bleeding disorders (31.9%), and abdominal pain/distention (26.9%) while less than 20% occurring for weakness (12.7%) and weight loss (10.5%). Table 5 shows the results of the physical examination at the first visit. Hepatomegaly was recorded in 5.6%, splenomegaly in 12.1%, lymphadenopathy in 10.8%, and 18.6% of the total patients had enlargement of all three organs, while 9.6% had hepatosplenomegaly and 4.3% had lymphadenopathy + H or S as well as 39% of all patients had no hyperplasia in the 3 organs (Table 5).

Table 1: Age and gender distribution of children with childhood leukemia in Sana'a, Yemen.

Sex	Total	
	No	%
Male	172	53.3
Female	151	46.7
Age groups		
1-5 years	23	7.1
6-10 years	219	67.8
11-15 years	81	25.1
Total	323	100
Mean age	7.96 years	
SD	3.93 years	
Median	8 years	
Mode	6 years	
Min	1 year	
Max	15 years	
Residency		
Urban	101	31.3
Rural	222	68.7

Table 2: Leukemia outcomes among children suffering from childhood leukemia in Sana'a, Yemen.

Outcomes	Frequency	
	No	%
Induction therapy	49	15.2
Consolidation (post-remission therapy)	14	4.33
Maintenance therapy	102	31.6
Relapse	7	2.2
*Cure	131	40.56
Died	20	6.19
Total	323	100

*Cure = 5-year survival rate = percentage of children who live at least 5 years after a diagnosis of leukemia.

Table 3: Age and gender wise distribution of various types of leukemia's among children suffering from childhood leukemia in Sana'a, Yemen.

Characters	Diagnosis					
	ALL		AML		Total	
	No	%	No	%	No	%
Gender						
Male	141	52.4	31	57.4	172	53.3
Female	128	47.6	23	42.6	151	46.7
Age groups						
1-5 years	18	6.7	5	9.2	23	7.1
6-10 years	178	66.2	41	75.9	219	67.8
11-15 years	73	27.1	8	14.8	81	25.1
Total	269	83.3	54	16.7	323	100

Table 4: The prevalence of clinical symptoms at the first visit among 323 children suffering from childhood leukemia in Sana'a, Yemen.

Symptoms	Frequency	
	No	%
Fever	253	78.3
Pallor	111	34.4
Bleeding disorders	103	31.9
Generalized body aches	89	27.6
Abdominal pain / distention	87	26.9
Weakness	41	12.7
Weight loss	34	10.5

Table 5: Findings of physical examination at the first visit among 323 children suffering from childhood leukemia in Sana'a, Yemen.

Signs	Frequency	
	No	%
Hepatomegaly	18	5.6
Splenomegaly	39	12.1
Lymphadenopathy	35	10.8
All 3 enlarged	60	18.6
Hepatosplenomegaly	31	9.6
Lymphadenopathy + H or S	14	4.3
No enlargement	126	39
Total	323	100
Total hepatomegaly	116	35.9
Total splenomegaly	137	42.4
Total lymphadenopathy	109	33.7

Discussion

Information about the prevalence of leukemia in the population may provide pathogenic hypotheses for disease control and assist in the effective management of leukemia and other hematological malignancies. In developing countries, especially in Yemen, there is little information about the burden and patterns of hematological malignancies, especially leukemia. In the current study, in relation to gender, the number of cases was slightly more male (53.3%), while the

percentage of female was 46.7% (male to female ratio=1.14-1). This result is similar to that reported in Africa where the male-to-female ratio is approximately equal, although slightly dominated by females (1:1.06) [31], but differs from that reported in the United States where the Cancer Society estimates American Leukemia in 2021, about 5690 new cases, 3000 in males and 2690 in females [32] and of those previously reported from Yemen where most cases were males (66.7%) while females were 33.3% (male to female ratio=2: 1) [33]. The present findings of different gender-specific leukemia prevalence rates contradict the facts that leukemia prevalence should vary by sex due to biological factors [13,34-36].

Leukemia may appear at all ages, from newborns to the elderly, but the distinctive forms have different age distributions [37]. In the current study, the mean age of \pm SD for all cases was 7.96 ± 3.93 years and most of the cases were in the age group 6-10 years (67.8%) (Table 1). This is roughly similar to what has been reported elsewhere for pediatric leukemia where the mean age of pediatric leukemia cases was 6.0 years with a peak incidence at 6-10 years [4,38,39]. This differs from the leukemia hypothesis with age in which older children may develop leukemia more frequently than younger children due to advancing age, as many environmental exposures to carcinogens, irradiation, and malignant mutations due to clonal expansion occur more often [40,41]. However, most of the younger children in the current study can be explained by the fact that prenatal and early life exposures are thought to be important determinants of pediatric leukemia. Several mechanisms have been identified through which exogenous and intrinsic factors can influence the risk of childhood leukemia. Exposure to a carcinogen or toxin early in a female's life may cause permanent damage. Since no new eggs are formed after birth and begin to mature during pregnancy, exposures that occur during this critical time can be of great importance. During pregnancy, exposure to factors such as ionizing radiation may act directly while others may act indirectly by transferring the placenta. On the other hand, offspring may be exposed after birth to environmental exposure, either directly or indirectly [42]. Since most of the children are from rural areas (68.7%) (Table 1), they may have been exposed to various environmental exposures during their stay with their parents who are farmers. Environmental factors, even though not well articulated, influence the chance of developing leukemia. In Yemen, rural residents' lifestyle is based on agricultural activities such as farming and plantations agriculture; especially Gat, fruits and vegetables plantation are the major practice around the study area, thus this may lead to the repeated use of chemicals such as pesticides, herbicides, and fertilizers for agricultural activities which will result in genetic mutations conferring leukemia [43]. In this study, acute lymphocytic leukemia was the most common, accounting for 83.3% of the total, while acute myelogenous leukemia counted 16.7% (Table 3). This result was consistent with results from Ethiopia, Nepal, and Pakistan [33,44], while it was contradictory with a study from Albania [45].

The clinical presentation of acute leukemia is vague and variable which makes it difficult to diagnose [46]. In this study, fever (78.3%), pallor (34.4%), bleeding disorders (31.9%), and abdominal pain/flatulence (26.9%) were found to be the most common complaints presented to patients at the first visit (Table 4). These are consistent results with Perveen

et al. and Kakibuto et al. studies [47,48]. Zaki et al. [49] Shahab and Raziq [50] mentioned that fever, bleeding and pallor are the main symptoms of complaints. These findings may be explained by the mechanism of leukemia as maturation block and/or suppression of erythrocytes and polymorph nuclear cells by increased production of blastocytes resulting in decreased/disordered production of normal leukocytes/neutrophils (leading to fever), and erythrocytes (leading to anemia/pallor) and platelets (leading to bleeding) [50]. Hepatomegaly was seen in 35.9% of patients, splenomegaly in 42.4% of patients and lymphadenopathy in 33.7% of patients. Enlargement of all three organs occurred in 18.6% of the total patients. Yasmeeen et al. [51] and Shahab and Raziq [50] reported elevated hepatomegaly (71%, 67%), splenomegaly (58%, 66%) and lymphadenopathy (75%, 71%). These results are consistent with the idea that patients in our area are in hospitals when the disease reaches an advanced stage [51]. This increase in the number of organ enlargements can be attributed to the fact that the study population was children and their organs can be easily observed if the slight increase in size is compared with the organs of adults.

Limitation of the Study

There were a number of limitations in this study. It was a retrospective, hospital-based study. There was selection bias because all cases were those that presented to the hospital. The hospital-based study also does not take into account the number of similar cases within the community, and therefore, estimates of the relative prevalence of specific diseases cannot be generalized. Data were taken from patient records that were filled in by different doctors, and were therefore not standardized.

Conclusion

ALL is the most common type of leukemia. The male-to-female ratio is roughly equal, and young children between the ages of 6-10 are most affected by leukemia. More comprehensive investigations of relevant factors and predictors using more recent diagnostic methods and investigation of association factors with valuation of the treatment protocols currently in use are needed.

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