

Childhood Leukemia in Yemen: The Main Types of Childhood Leukemia, its Signs and Clinical Outcomes

Abdulrahman M Alhadi¹, Monya Abdullah Yahya El-Zine², Abdulrahman A IshaK¹ and Hassan A Al-Shamahy^{3*}

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

²Department of Histopathology, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen

³Medical Microbiology and Clinical Immunology Department, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen

***Corresponding Author:** Hassan A Al-Shamahy, Professor, Medical Microbiology and Clinical Immunology Department, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen.

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Abstract

Background and Aims: Childhood leukemia is one of the leading causes of morbidity and mortality in the pediatrics age group. Despite its high fatality rate, less attention has been paid to the problem in developing countries, including Yemen. For this reason, childhood leukemia is not well documented in the study setting. Therefore, we assessed the prevalence of different types of leukemia, clinical signs and its association with sex and ages in Yemen.

Patients and Methods: A descriptive observational study was conducted on children with leukemia who were treated selectively in the pediatric leukemia units of Al-Kuwait University Hospital in Sana'a. Group diagnoses and histopathological diagnoses were formed in line with the French, American and British classifications of childhood leukemia in pediatric leukemia units, over a period of 5 years from January 1, 2014 to December 31, 2018. The study variables were qualitative (types of leukemia, gender, clinical signs, outcomes) and quantitative (age).

Results: 244 leukemia patients were diagnosed, treated and followed up with mean \pm SD age = 6.44 ± 3.7 years, most of the cases were in the age group 1 - 5 years (50%) and male were predominant (66.7%). Acute lymphoblastic leukemia (ALL) was the most common (78.6%), followed by acute myelogenous leukemia (AML) (15.6%), while chronic myelogenous leukemia (CML) (4.5%) and Juvenile myelomonocytic leukemia (JML) (1.2%) were rare. All was predominant in the age group 1 - 5 years (50%), while CML was predominant in the age group 11 - 15 years (42%), while CML was roughly evenly distributed in all age groups. Symptoms in the different types of leukemia in children include symptoms that occurred in more than 50% as fever, rash, loss of appetite and recurrent infections (53.1%). In respect to the outcomes, the cure rate was 40.7%, the death rate was 6.2%, the relapse rate was 2%. The rest of the cases were in maintenance therapy (31.5%), induction therapy (15.4%) and consolidation (4.3%).

Conclusion: All is the most common type of leukemia in Sana'a city and males and young children are affected the most by leukemia. Symptoms in the different types of childhood leukemia in the current study are similar to those reported elsewhere and the cure rate was good and the death rate was low. Although childhood leukemia in Yemen is not receiving much attention from local policymakers, the prevalence of childhood leukemia is still prevalent in the study environment. Meanwhile, an increasing number of reported cases may occur with increased awareness, knowledge, diagnostic tools and affordability. Therefore, a large-scale, community-based study should be conducted to address these children who have not yet made the access gate.

Keywords: Childhood Leukemia; Clinical Outcomes; Signs; Types; Yemen

Introduction

Leukemia is a heterogeneous cluster of hematologic malignancies to includes several diverse and biologically distinct sub-clusters. It is a clonal tumor of hematopoietic cells consequential from ranges of factors that lead to somatic mutations in progenitor cells and pluripotent stem cells. The metamorphic tumor cells behave like hematopoietic stem cells as they can self-reproduce, differentiate and feed progenitor cells in different hematopoietic lineages. These single-strength leukemia stem cells can undergo varying degrees of maturity to phenotypic copies of mature blood cells [1,2]. Childhood leukemia is a type of childhood cancer and it is the most frequent type of cancer in childhood, reporting for 29% of cancers in children aged 0 - 14 in 2018 [3]. Depending on the type of cell, leukemia develops from the cells and how mature the cells are, a group of French, American and British leukemia experts in the 1970s divided myeloid leukemia into acute myeloid leukemia (AML with subtypes, M0 to M7) and chronic myeloid leukemia (CML) and myelodysplastic syndromes (MDS). This was mainly dependent on how the leukemia cells appeared under the microscope after routine staining and some cytochemical properties [4-6]. Acute myeloid leukemia (APL) is a specific type of acute myeloid leukemia. In this leukemia, the promyelocytes are produced and accumulated in the bone marrow. Chromosome-specific transmission has been found in APL patients. The genes on chromosome 15 change where the genes are located on chromosome 17. This genetic change prevents promyelocytes from maturing properly [7].

CML is chronic leukemia that progresses gradually over months to years. Chronic myeloid leukemia is rare in children, but it does happen [8]. Patients with CML have too many immature white blood cells and the cells gathering with other healthy blood cells and chromosome translocation occurs in the patients. Also, part of chromosome 9 breaks off and attaches to chromosome 22, which facilitates the exchange of genetic material between chromosomes 9 and 22 in their cells. Chromosome rearrangements alter the locations and functions of certain genes, which leads to uncontrolled cell growth [7]. Chronic lymphocytic leukemia (CLL) is another form of chronic leukemia, but it is very infrequent in children [9]. Juvenile myelomonocytic leukemia (JMML) the myelomonocytic cells in the bone marrow are overproduced. It is sometimes considered a myeloproliferative tumor. It is rare and occurs more commonly in children under the age of four. Myelomonocytic cells produced by the bone marrow invade the spleen, lungs and intestine in JMML [10,11].

On the other hand, in Yemen as in the majority of Arab countries, there are few specialized epidemiological records dedicated to this field and for that reason it is important to encourage, update, build up and continue to offer studies on the manners of childhood leukemia with the purpose of achieve a greater extent and influence on public health, with early diagnosis and suitable treatment with the purpose of enhance survival and reduce possible subsequent consequences. According to the Limited Yemen Cancer Studies, the most common cancer among Yemeni children and adults were leukemia (33.1%), lymphoma (31.5%), central nervous system tumors (7.2%) and bone tumors (5.2%) [12-14]. This study was performed to give base line description of childhood leukemia pattern of recorded in Al-Kuwait university hospital in Sana'a city. These registers are not population-based cancer registration but is the only available source. We served to prove the basic demographic, the prevalence of different types of leukemia, clinical signs, outcomes and its association with sex and ages which can be competed with available studies on literatures. On other hand to provide primary base line tool to work-up for future population studies on childhood leukemia in Yemen.

Patients and Methods

A descriptive observational study for 5 years interval between January 2010 - December 2014. The study was conducted on children with leukemia who were treated in the pediatric leukemia units of Al-Kuwait University Hospital in Sana'a. The diagnosis of cases was based on clinical examination by a specialist (signs and symptoms that indicate that the child may have leukemia such as swollen lymph nodes, areas of bleeding, bruising, etc.) Which confirmed by blood film examination and histological bone marrow study. The study variables were qualitative (types of leukemia, gender, clinical signs, outcomes) and quantitative (age). Group diagnoses and histopathological diagnoses were formed in line with the French, American and British classifications (FAB) of childhood leukemia [4-6].

Statistical analysis

Data were reported using appropriate descriptive statistics (including frequency, mean, and standard deviation. The patient data were entered using Epi info version 7 for analysis. The data analysis including demographic data, clinical signs and symptoms; types of leukemia' and outcomes. We presented the results by using tables and figures.

Ethical approval

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

Results

Table 1 shows the age and gender distribution of children with childhood leukemia in Sana'a, Yemen. The mean ± SD age of all cases was 6.44 ± 3.7 years. Most of the cases were in the age group 1 - 5 years (50%), followed by the age group 6 - 10 years (32.1%), while only 17.9% of the cases were in the age group 11 - 15 years (disease decreases with increasing age). As for gender, most of the cases were males (66.7%), while the percentage of females was 33.3% (male to female ratio = 2 - 1). Table 2 shows the distribution of leukemia types among children with childhood leukemia in Sana'a, Yemen. Acute lymphoblastic leukemia was the most common, accounting for 78.6% of the total, while the other types were less common, with acute myelogenous leukemia count of 15.6%, chronic myelogenous leukemia at 4.5% and Juvenile myelomonocytic leukemia only at 1.2%. Table 3 shows the relationship between leukemia types and age groups of affected children. ALL was predominant in the age group 1 - 5 years (younger children (50%), while chronic myeloid leukemia was predominant in the age group 11 - 15 years (42%), while chronic myeloid leukemia was roughly evenly distributed in all age groups. JCM was rare and 2 cases were reported in the 1 - 5 year group and one case was in the 11 - 15 year group. The mean age of the oldest with AML patients (8.3 years), while with ALL patients was 6.2 years. Table 4 shows frequency of clinical symptoms among 244 children suffering from childhood leukemia in Sana'a, Yemen. Symptoms in the different types of leukemia in children in the current study include symptoms that occurred in more than 50%: fever (54.9%) rash (54.9%), loss of appetite (50%) and recurrent infections (53.1%); While others are less common they include: ease of bleeding (35.8%), feeling tired or weak (42.6%), bone and joint pain (45.7%), abdominal pain or fullness (34%), and enlarged lymph nodes under the arms, in the groin. and chest and neck (43.8%). Table 5 shows leukemia outcomes among children suffering from childhood leukemia in Sana'a, Yemen. The cure rate was 40.7% while the death rate was 15 cases (6.2%), all of them male (male mortality rate = 9.3%). The relapse rate was 2%. The rest of the cases were in maintenance therapy (31.5%), induction therapy (15.4%), and consolidation (post-remission therapy) for 4.3% of cases.

Age groups	Male		Female		Total	
	No	%	No	%	No	%
1 - 5 years	75	46.3	47	24.1	122	50
6 - 10 years	57	41	21	25.9	78	32.1
11 - 15 years	30	18.5	14	16.7	44	17.9
Total	162	66.7	82	33.3	244	100
Mean age	6.7 years		5.8 years		6.44 years	
SD	3.6 years		3.7 years		3.7 years	
Median	6 years		1 years		6 years	
Mode	3 years		3 years		3 years	
Min	1 year		1 year		1 year	
Max	15 years		14 years		15 years	

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

Leukemia types	Male		Female		Total	
	No	%	No	%	No	%
ALL	131	80.6	61	74.4	192	78.6
AML	27	16.7	11	13	38	15.6
CML	4	2.8	7	9.3	11	4.5
JCM	0	0	3	3.7	3	1.2
Total	162	66.7	82	33.3	244	100

Table 2: Distribution of leukemia types among children suffering from childhood leukemia in Sana'a, Yemen. ALL: Acute Lymphoblastic Leukemia; AML: Acute Myelogenous Leukemia; CML: Chronic Myelogenous Leukemia; JCM= Juvenile Myelomonocytic.

Age groups	ALL		AML		CML		JCM		Total	
	No	%	No	%	No	%	No	%	No	%
1 - 5 years	102	53.5	14	36.8	4	36.3	2	66.7	122	50
6 - 10 years	67	34.8	8	21	3	27.3	0	0	78	32.1
11 - 15 years	23	11.9	16	42	4	36.4	1	33.3	44	17.9
Total	192	78.6	38	15.6	11	4.5	3	1.2	244	100
Mean age	6.2 years		8.3 years		6.2 years		7.5 years		6.44 years	
SD	3.4 years		3.4 years		4.7 years		7.8 years		3.7 years	
Min	1 year		1 year		1 year		2 year		1 year	
Max	15 years		15 years		14 years		13 years		15 years	

Table 3: Relationship between leukemia types and age groups of affected children. ALL: Acute Lymphoblastic Leukemia; AML: Acute Myelogenous Leukemia; CML: Chronic Myelogenous Leukemia; JCM: Juvenile Myelomonocytic.

Symptoms	Number	Percentage
Fever	134	54.9
Easy bleeding	78	35.8
Swollen lymph nodes	107	43.8
Bone and joint pain	111	45.7
Abdominal pain or fullness	85	34
Anemia	84	34.6
Loss of appetite	122	50
Periapism	32	8
Feelings of fatigue	104	42.6
Repetitive infections	129	53.1
Rash	134	54.9

Table 4: Frequency of clinical symptoms among 162 children suffering from childhood leukemia in Sana'a, Yemen.

Outcomes	Male		Female		Total	
	No	%	No	%	No	%
Induction therapy	24	14.8	13	16.	40	15.4
Consolidation (post-remission therapy)	9	5.6	2	2.4	11	4.3
Maintenance therapy	48	29.6	29	35.3	77	31.5
Relapse	2	0.9	3	3.7	5	2
*Cure	64	39.8	35	42.6	99	40.7
Died	15	9.3	0	0	15	6.2
Total	162	66.4	82	33.6	244	100

Table 5: Leukemia outcomes among children suffering from childhood leukemia in Sana’a, Yemen.

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

With ALL or AML, children who are free of the disease after 5 years are very likely to be cured, because it is very rare for these cancers to return after this long period.

Discussion

One of the most common types of cancer in children is leukemia, accounting for 25 - 30% of all types of cancer in children and adolescents [3,15,16]. In the current study, the mean ± SD age of all cases was 6.44 ± 3.7 years with a median of 6 years; most of the cases were in the 1 - 5 year age group (50%) (Table 1). This finding is similar to that reported by the National Cancer Institute in which childhood leukemia is most commonly diagnosed in children between the ages of 1 to 4 years old with the median age of diagnosis is 6 years old [15]. In the current study for gender, most of the cases were male (66.7%), while the female rate was 33.3% (male to female ratio = 2 - 1). This finding is similar to that reported in other settings in the world where leukemia in children is more common in boys than in girls [3,4,15]. In the current study, acute lymphocytic leukemia was the most common, accounting for 78.6% of the total (Table 2) and this is consistent with findings from Atlanta: American Cancer Society [9], Dana Farber Boston and pediatric cancer and blood disorders center reports [8], which stated that ALL is the most common type of leukemia in children, accounting for 75 - 80% of diagnostic cases. In this study, the number of acute myelogenous leukemia was 15.6% of the total (second common) and this is similar to the facts that AML is the second most common type of leukemia in children after ALL and makes up most of the remaining diagnoses of leukemia [8]. In the current study, AML was prevalent in the age group 11 - 15 years (42%) and in male patients than in females (Table 2) and this differs from that reported elsewhere in the world where AML is most commonly diagnosed in children who are under one year. Unlike ALL, it occurs equally between boys and girls and also occurs equally among racial/ethnic groups [17,18]. In the current study, chronic myelogenous leukemia was rare (4.5%) (Table 2). CML is chronic leukemia that develops slowly over months to years. CML is rare in children, but it does occur [8]. Patients with CML have too many immature white blood cells, and the cells crowd with other healthy blood cells. Chromosome translocation occurs in CML patients. Part of chromosome 9 separates and attaches to chromosome 22, which facilitates the exchange of genetic material between chromosomes 9 and 22. Chromosome rearrangements alter the locations and functions of specific genes, which leads to uncontrolled cell growth [7]. Additionally, in the current study, JMML was rare (1.2%) (Table 2). JMML is a form of leukemia in which the myelomonocytic cells are overproduced. It is sometimes considered a myeloproliferative tumor and is rare and occurs more commonly in children under the age of four. In JMML, myelomonocytic cells produced by bone marrow invade the spleen, lungs and intestine [10,11].

Most of the primary symptoms of leukemia are associated with problems with bone marrow function. There are a multiplicity of symptoms that children may experience. Symptoms tend to emerge quickly in acute leukemia and slowly over time in chronic leukemia [3]. Symptoms and signs in the different types of leukemia in children in the current study include symptoms that occurred in more than

50%: fever (54.9%), rash (54.9%), loss of appetite (50%) and recurrent infections (53.1%); While others are less common they include: ease of bleeding (35.8%), feeling tired or weak (42.6%), bone and joint pain (45.7%), abdominal pain or fullness (34%) and enlarged lymph nodes under the arms, in the groin. and chest and neck (43.8%) (Table 4). This range is similar to what has been reported in previous studies in different parts of the world [3,7,9,19-21].

In this study the cure rate (5-year survival rate) was 40.7% while the death rate was 6.2% (15 cases) all male (male mortality rate = 9.3%). The relapse rate was 2%. The rest of the cases were maintenance therapy (31.5%), induction therapy (15.4%), and consolidation (post-remission therapy) for 4.3% of cases. The 5-year survival rate refers to the percentage of children who live at least 5 years after their leukemia is diagnosed. With acute leukemia (ALL or AML), children who have abandoned the disease after 5 years are very likely to be cured, since it is very rare for these cancers to return after this long time [22]. The 5-year survival rate for children with AML has also improved over time and is now in the extent of 65% to 70%. Nevertheless, survival rates vary depending on the AML subtype and other factors. For example, most studies indicate that the cure rate for acute myeloid leukemia (APL), a subtype of AML, is now higher than 80%, but rates are lower for some other subtypes of AML [15,19,23,24]. Though, for JMML, 5-year survival rates have been reported to be around 50% [25] and for CML, which is rare in children, 5-year survival rates are less beneficial, because some children may live long with chronic myeloid leukemia without being treated. In the past, 5-year survival rates for CML have been reported in the range of 60% to 80%. But with newer and more effective drugs used to treat CML in recent years, survival rates are likely to be higher now [25-27]. Finally, the 5-year survival rate for children with leukemia is 83.6% in the USA and in developed countries and this means that 83.6% of children with leukemia live for 5 years or more after diagnosis. In doing so, this was significantly improved from the 5-year survival rate of 36.5% in 1975. The progress is largely approved to advances in treatment, especially treatment of ALL [9,19]. The position or prognosis of a child is affected by the type of leukemia. Additionally, there are certain patient characteristics and types of cancer that help clinicians expect the prognosis (and determine treatment). These are referred to as prognostic factors. Prognostic factors are generally of greater significance in ALL than in AML [5,24].

Conclusion

ALL is the most common type of leukemia in Sana'a city; and males and young children are affected the most by leukemia. Symptoms in the different types of childhood leukemia in the current study are similar to those reported elsewhere and the cure rate was good and the death rate was low. Although childhood leukemia in Yemen is not receiving much attention from local policymakers, the prevalence of childhood leukemia is still prevalent in the study environment. Meanwhile, an increasing number of reported cases may occur with increased awareness, knowledge, diagnostic tools and affordability. Therefore, a large-scale, community-based study should be conducted to address these children who have not yet made the access gate.

Conflict of Interest

No conflict of interest associated with this work.

Author's Contribution

The first author presented the data and the first, second and the third authors analyzed the data and wrote, revised and edited the paper.

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