Clinical Characteristics and Outcome After Induction of Chemotherapy in Pediatric Acute Lymphoblastic Leukemia: A Descriptive and Correlational Study From the West Bank of Palestine

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Research article

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Abstract

Background

Pediatric acute lymphoblastic leukemia (ALL) is the most prevalent type of cancer among children. This study was conducted to describe and correlate the clinical characteristics and outcomes of treatment of patients with pediatric ALL in the main referral hospital in Palestine.

Methods

In this single-center, retrospective, observational study, paper-based and electronic medical records of patients with pediatric ALL who received induction chemotherapy were reviewed. The sociodemographic variables, details of patient history, findings of physical examinations, daily progress notes, bone marrow biopsies, flow cytometry, and cytogenetics of patients were collected.

Results

Complete data of 69 patients were included in this analysis. The majority (79.7%) of the patients had B-ALL phenotype, 22 (31.9%) had abdominal pain, 37 (53.6%) had fever, 30 (43.5%) complained of bone pain, 50 (72.5%) had pallor, 9 (13.0%) had anorexia, 34 (49.3%) had hepatomegaly, 34 (49.3%) had splenomegaly, and 15 (21.7%) complained of bleeding symptoms. After induction chemotherapy, remission was experienced by the vast majority of the patients and 5 (7.2%) experienced relapse after receiving chemotherapy. The vast majority of the patients (96%) had CNS status 1, 1.4% had CNS status 2, and 2.9% had CNS status 3. Cytogenetics for patients with B-ALL phenotype indicated that 10 (18.2%) patients had t(12,21) translocation, 5 (9.1%) had hyperdiploidy, 4 (7.3%) had t(1,19) translocation, and 2 (3.6%) had t(9,22) translocation. The initial white blood cells (p value < 0.001), absolute neutrophils (p value = 0.011), and hemoglobin (p value < 0.001) were significantly lower for patients with B-cell ALL. Platelet counts were significantly lower (p value = 0.012) in patients with splenomegaly and those with bleeding symptoms (p value = 0.008). Presence of pallor was positively associated (p value = 0.035) with T-cell ALL. Presence of hepatomegaly was positively associated (p value < 0.001) with splenomegaly.

Conclusion

Overall, this study provides insights into the clinical characteristics and outcomes of induction chemotherapy in Palestinian patients with pediatric ALL. The characteristics of ALL among Palestinians were comparable to their peers in the region. The outcomes of induction chemotherapy were also comparable to other published data for ALL patients.

Background

Cancer is the second most common cause of mortality among Palestinians in the West Bank and Gaza Strip [1]. In general, leukemias are the most common types of cancers among Palestinian children with an estimated incidence rate of 2.6 per 100,000 children [1, 2]. Acute lymphoblastic leukemia (ALL) is the most diagnosed tumor in pediatric populations and the most frequent cause of death from cancer before the age of 20 [3]. According to some estimates, more than 75% of pediatric leukemias are ALL. One annual basis, about 6,000 ALL cases are diagnosed in the US, of those, about 50% are children and teenagers [4, 5]. In the US, ALL is more common in Caucasians and Hispanics compared to African Americans [6]. Reports on the prevalence of pediatric ALL in the Middle East, especially, among the Palestinian population are scarce [2]. The Middle East Childhood Cancer Alliance (MECCA) collected clinical and demographic data on children with ALL from 16 countries in the Middle East [7]. It is noteworthy mentioning that Palestinians were not included in the MECCA's study [7].

ALL is a result of clonal proliferation of early lymphoid precursors (lymphoid stem or progenitor cells) with arrested maturation [8, 9]. ALL occurs more frequently in B-lineage (B-cell precursor immunophenotype or B-ALL) compared to T-lineage (T-cell precursor immunophenotype or T-ALL) [9]. Of patients with pediatric ALL, approximately 80% have B-ALL [7, 10, 11]. On the other hand, patients with T-ALL comprise about 10%-15% the patients. Historically, patients with pediatric T-ALL showed lower cure rates [12].

Structural mutations of the chromosomes including aneuploidy and translocations are characteristic features in ALL. The World Health Organization (WHO) classifies B-ALL on the basis of molecular and cytogenetic characteristics [13]. Aneuploidy include high-hyperdiploid (chromosomes ≥ 51) and hypodiploid (chromosomes ≤ 44) and translocations include t(12;21)/*ETV6-RUNX1*, t(1;19)/*TCF3-PBX1*, t(9;22)/*BCR-ABL 1*, and *KMT2A* rearrangement [11, 14, 15]. Currently, 9 subtypes have been identified and classified by specific translocations on chromosomes, rearrangements, and ploidy status [9, 11, 13]. Historically, subtypes of ALL are shown to be associated with variable risk of disease progression and response to treatment options [16-18].

Clinical presentation of ALL may include fever, signs indicative of anemia (for example: pallor, tachycardia, fatigue, and headache), increased risk of infection, and bleeding [19, 20]. Currently, protocols of treatment stratify patients by risk to receive chemotherapy of multiple agents that can lead to cure rates of up to 90% in countries with high income [17]. It is noteworthy mentioning that despite the initial response to therapy, 10-15% of the patients experience relapse. This relapse is considered one of the leading causes of mortality in childhood cancers [21, 22]. Therefore, early diagnosis and optimizing prognosis are of crucial importance.

Diagnosis of pediatric ALL is often based on physical examination, complete blood count, and blood smears. In the majority of cases, blast cells are seen on blood smears. Biopsies of bone marrow are also used to provide a conclusive diagnosis [23]. Lumbar punctures could also be used to determine involvement of the central nervous system [24]. Additionally, complete blood count, clinical findings, and cytogenetics are frequently used in deciding on the risk-stratified and multi-agent chemotherapy [15, 17, 20, 25].

Description of epidemiological and clinical characteristics of patients with ALL in different nations has received considerable attention [26]. In Palestine, cancer care is highly fragmented and a high percentage of patients receive treatment outside the country [1, 27]. Currently, referral hospitals in which patients

with pediatric ALL receive induction chemotherapy in Palestine are limited [1, 27]. Since its inception, An-Najah National Hospital has emerged as the main referral hospital for pediatric ALL in Palestine.

Ayesh et al determined the frequency of thiopurine methyltransferase polymorphisms and whether polymorphisms were associated with side effects of 6-mercaptopurine using 56 DNA samples from patients with pediatric ALL in Gaza Strip [28]. Abuhelwa et al reported the characteristics of patients with de novo acute myeloid leukemia in Palestine [29]. However, little is known on the clinical characteristics and outcomes of induction chemotherapy among patients with pediatric ALL in Palestine. Therefore, this study was conducted to describe the clinical characteristics and outcomes of induction chemotherapy among patients with pediatric ALL in the main referral hospital in Palestine. The study also aimed to assess associations between sociodemographic and clinical characteristics of the patients included in the study.

Methods

Study site

The study was conducted at An-Najah National Hospital, Nablus. Since its inception in 2014, An-Najah National Hospital has become the main referral care center for patients with pediatric ALL and adult leukemias in Palestine. The hospital has an active oncology department in which about 800 patients from the West Bank of Palestine and Gaza Strip receive treatment for different cancers on annual basis.

Study participants

Patients with pediatric ALL were included in this study. The inclusion criteria were: a) patients who were 16 years old and younger, b) admitted to the referral hospital with a diagnosis of pediatric ALL, and c) received induction chemotherapy at the study site. We did not restrict inclusion based on gender or admission dates. Therefore, all patients of both genders who were admitted to the study site from its inception (January 2014) to January 2018 were included in the present study. Patients with incomplete medical records and those who received their induction chemotherapy outside the referral hospital were excluded from the study.

Study design, tools, and collection of data

This present study was a single-center, retrospective, observational study. The study used a descriptive-correlational approach. In this study, paper-based and electronic medical records of patients with pediatric ALL were reviewed by field researchers. A data collection form that was created for this study using Excel Spreadsheets (Microsoft Excel, Microsoft Inc, US) was used to extract the pertinent data (Additional file 1). The data collected for this study were informed by previous studies [7, 29, 30]. The data collected for the purpose of this study included: sociodemographic variables like age and gender, detailed patient history, detailed findings of the physical examination, and daily progress notes of each patient. Hematological reports were reviewed and hemoglobin levels, platelet counts, initial white blood cells (WBCs) counts, and absolute neutrophils counts were collected. Clinical characteristics like presence of abdominal pain, fever, bone pain, central nervous system (CNS) status, fatigue, anorexia, hepatomegaly, splenomegaly, and bleeding symptoms were also collected. The data collection form also collected information relevant to bone marrow biopsies, flow cytometry, and cytogenetics (Additional file 1). Data were collected from the time the patient was admitted until outcomes of induction became available. The outcomes of the induction were assessed based on the bone marrow biopsies performed on days 19-21 after initiation of induction chemotherapy. In this study, the outcomes were classified as follows: a) remission ($< 5\%$ blasts on bone marrow), b) non-remission ($\geq 5\%$ blasts on bone marrow), c) relapse ($\geq 20\%$ blasts in bone marrow, any blasts in CNS or both), or d) death of the patient during the first admission for the induction chemotherapy.

Ethical approval

The protocol and ethics of this study were approved by the Institutional Review Board (IRB) of An-Najah National University under the archived number (IRB-20-2017). Data and information leading to the identity of the patient were not collected into the data collection form. The data were coded during the data analysis.

Statistical analysis

Data were entered into IBM SPSS for Windows v.21.0 (IBM Inc. Armonk, New York). Kolmogorov–Smirnov test was used to assess whether the data were normally distributed or not. Because the data were not normally distributed, the data were expressed using medians and their corresponding interquartile range (IQR). Categorical data were compared using Mann-Whitney *U* test. Correlation was investigated using Spearman's rank correlations. Statistical significance was considered when the *p* value was < 0.05 .

Results

All medical records of patients who received induction chemotherapy at An-Najah National Hospital were reviewed. Complete records and laboratory reports were identified for a total of 69 patients. Patients with complete records and laboratory reports were included in the final analysis.

Sociodemographic and clinical characteristics of the study patients

The median age of the patients at presentation was 6.0 with an IQR of 3.5 years. Of all patients, 26 (37.7%) were younger than 10 years of age, and 43 (62.3%) were at least 10 years of age or older. Of the patients included, 42 (60.9%) were male and 27 (39.1%) were female in gender. With regard to the signs and symptoms at presentation, 22 (31.9%) patients had abdominal pain, 37 (53.6%) had fever, 30 (43.5%) complained of bone pain, 50 (72.5%) had pallor, 9 (13.0%) had anorexia, 34 (49.3%) had hepatomegaly, 34 (49.3%) had splenomegaly, and 15 (21.7%) complained of bleeding symptoms. After induction of chemotherapy, 5 (7.2%) patients experienced relapse after receiving treatments. The vast majority of the patients (96%) had CNS status 1, 1.4% had CNS status 2, and 2.9% had CNS status 3. The majority of the patients had B-ALL (79.7%) and 20.3% had T-ALL. Details of the sociodemographic and clinical characteristics of the patients are shown in Table 1.

Cytogenetic studies for the B-ALL phenotype showed that 10 (18.2%) patients had t(12,21) translocation, 5 (9.1%) had hyperdiploidy, 4 (7.3%) had t(1,19) translocation, and 2 (3.6%) had t(9,22) translocation. Of all patients, 19 (34.5%) did not have any of the previously mentioned abnormal cytogenetics (Table 1).

Table 1: Sociodemographic and clinical characteristics of the patients with pediatric ALL included in the study (*n* = 69)

Characteristic	n	%
Age (years)		
< 10	26	37.7
≥ 10	43	62.3
Gender		
Male	42	60.9
Female	27	39.1
Presence of abdominal pain		
Yes	22	31.9
No	47	68.1
Presence of fever		
Yes	37	53.6
No	32	46.4
Presence of bone pain		
Yes	30	43.5
No	39	56.5
CNS status¹		
CNS 1	66	95.7
CNS 2	1	1.4
CNS 3	2	2.9
Presence of pallor		
Yes	50	72.5
No	19	27.5
Presence of anorexia		
Yes	9	13.0
No	60	87.0
Presence of hepatomegaly²		
Yes	34	49.3
No	35	50.7
Presence of splenomegaly³		
Yes	34	49.3
No	35	50.7
Presence of bleeding⁴		
Yes	15	21.7
No	54	78.3
Immunophenotype		
B-ALL	55	79.7
T-ALL	14	20.3
Cytogenetics for B-ALL		
t(12,21)	10	18.2
Hyperdiploidy	5	9.1
t(1,19)	4	7.3
t(9,22)	2	3.6

Characteristic	n	%
Nil	19	34.5
Missing	15	27.3
Relapse⁵		
Yes	5	7.2
No	64	92.8
Remission⁶		
Yes	68	98.5
No	1	1.5

¹CNS1: WBC in CSF ≤ 5 without WBC blasts, CNS2: WBC in CSF ≤ 5 with WBC blasts, CNS3: WBC in CSF ≤ 5 with WBC blasts; ²Hepatomegaly: palpable liver below the costal margin; ³Splenomegaly: palpable spleen; ⁴Presence of bleeding symptoms like petechiae, epistaxis, bruising, gum bleeding, blood in stool; ⁵Relapse: Patient was in remission and developing any of the following: 1. More than 20% of blasts in bone marrow, or, 2. CNS status 2 or 3, or, 3. Both 1 + 2; ⁶Remission: The percentage of blast cells in the bone marrow is less than 5% at the end of induction of chemotherapy.

Hematological laboratory data at admission

The median hemoglobin at admission was 9.00 with an IQR of 2.70 g/dL. The median platelet count was 80,000 with an IQR of 157,000 platelets/mm³. For the initial WBCs count, the median was 7,100 with an IQR of 20,600 cells/mm³. For the absolute neutrophils count, the median was 1,420 with an IQR of 2,030 cells/mm³. The detailed hematological laboratory data of the study participants are shown in Table 2.

Table 2: Hematological laboratory data at admission (n=69)

Statistic	Hemoglobin (g/dL)	Platelet count (per mm ³)	Initial WBCs count (cells/mm ³)	Absolute neutrophils count (cells/mm ³)
Median	9.00	80000	7100	1420
IQR	2.70	157000	20600	2030

IQR: interquartile range, WBCs: white blood cells

Association between the different sociodemographic and clinical characteristics of the study patients with their hematologic laboratory findings

The median hemoglobin in patients who were 5 years of age and older (9.1 with an IQR of 2.5 g/dL) was significantly higher (p value = 0.007) than those who were younger than 5 years (7.8 with an IQR of 2.8 g/dL). The median platelet count in patients who did not have splenomegaly (122,000 with an IQR of 169,000) was significantly higher (p value = 0.012) than those who had splenomegaly (49,500 with an IQR of 145,850). The median platelet count for patients who did not have bleeding symptoms (103,000 with an IQR of 171,000) was significantly higher (p value = 0.008) than those who had bleeding symptoms (34,000 with an IQR of 66,050). The median hemoglobin for patients who had T-ALL (11.2 with an IQR 2.8) was significantly higher (p value < 0.001) than those who had B-ALL (8.4 with an IQR of 2.5). The median initial WBCs count for patients who had T-ALL (22,100 with an IQR 35,550) was significantly higher (p value < 0.001) than those who had B-ALL (5,000 with an IQR of 10,950). The median absolute neutrophil count for patients who had T-ALL (2,670 with an IQR of 4,595) was significantly higher (p value = 0.011) than those who had B-ALL (1,050 with an IQR 1,730). Other variables were not significantly associated (p value > 0.05). The details of associated variables are shown in Table 3.

Table 3: Association between sociodemographic and clinical characteristics and hematologic findings of patients with pediatric ALL

	Hemoglobin (g/dL)						Platelet count				Initial WBC count				Age (years)
Characteristic	n	%	Median	IQR	Mean rank	P value	Median	IQR	Mean rank	P value	Median	IQR	Mean rank	P value	Median
Age (years)															
< 10	26	37.7	7.8	2.8	26.6	0.007	57000	93000	30.2	0.119	7700	26400	37.3	0.454	17
≥ 10	43	62.3	9.1	2.5	40.1		118500	167000	37.9		4600	11028	33.6		14
Gender															
Male	42	60.9	8.5	3.0	38.3	0.088	87000	162500	36.1	0.563	7100	18700	38.4	0.077	16
Female	27	39.1	9.0	3.6	29.9		67000	171000	33.3		5000	7550	29.7		94
Presence of abdominal pain															
Yes	22	31.9	9.0	3.5	34.2	0.822	88500	179000	35.6	0.867	5100	10670	36.4	0.690	13
No	47	68.1	8.8	3.0	35.4		64000	167000	34.7		7100	16700	34.3		15
Presence of fever															
Yes	37	53.6	9.0	2.6	37.8	0.217	78000	155250	34.7	0.909	4900	17178	34.8	0.942	13
No	32	46.4	8.5	2.5	31.8		64000	180500	35.3		7700	13950	35.2		15
Presence of bone pain															
Yes	30	43.5	9.1	2.9	34.8	0.928	59000	123000	33.2	0.506	5300	13100	33.4	0.553	16
No	39	56.5	8.7	2.2	35.2		88500	185500	36.4		5650	16725	36.3		93
Pallor															
Yes	50	72.5	8.5	2.8	32.6	0.111	84000	157000	35.9	0.537	5300	13970	34.0	0.515	14
No	19	27.5	9.4	3.5	41.2		65500	211800	32.6		7300	19750	37.6		14
Presence of anorexia															
Yes	9	13.0	8.3	2.6	30.3	0.449	121000	168000	37.3	0.708	17700	32350	40.8	0.354	15
No	60	87.0	9.0	2.5	35.7		71000	158000	34.7		5000	12643	34.1		14
Presence of hepatomegaly															
Yes	34	49.3	9.0	1.6	36.1	0.644	50000	144500	31.5	0.151	5000	15750	36.6	0.513	14
No	35	50.7	8.3	3.8	33.9		118500	173000	38.4		6350	14350	33.4		14
Presence of splenomegaly															
Yes	34	49.3	9.0	1.7	37.1	0.381	49500	145850	28.8	0.012	7200	24300	38.0	0.216	16
No	35	50.7	7.8	3.0	32.9		122000	169000	41.0		5200	9250	32.1		10
Presence of bleeding															
Yes	15	21.7	8.0	4.5	30.6	0.333	34000	66050	22.9	0.008	9600	12335	39.1	0.367	16
No	54	78.3	8.9	2.2	36.2		103000	171000	38.4		4900	15300	33.9		13
Immunophenotype															
B-cell ALL	55	79.7	8.4	2.5	30.0	<0.001	72000	156000	34.3	0.546	5000	10950	30.6	<0.001	10
T-cell ALL	14	20.3	11.2	2.8	54.6		97500	264600	37.9		22100	35550	52.3		26
Relapse ⁵															
Yes	5	7.2	7.8000	1.35	31.8	0.711	60500	166750	38.2	0.711	1290	12353	24.7	0.233	29
No	64	92.8	9.0000	2.80	35.3		84000	166000	34.8		5600	14500	35.8		15

Correlation between sociodemographic and clinical characteristics of patients with pediatric ALL

There was a positive correlation (p value = 0.035) between presence of pallor at presentation and T-ALL immunophenotype. Again, there was a positive correlation (p value < 0.001) between presence of hepatomegaly and presence of splenomegaly. Other variables were not significantly correlated (p value > 0.05). The detailed correlations are shown in Table 4.

Table 4: Correlation between sociodemographic and clinical characteristics of patients with pediatric ALL

Characteristic	Correlation	Presence of abdominal pain	Presence of fever	Presence of bone pain	CNS status	Presence of pallor	Presence of anorexia	Presence of hepatomegaly	Presence of splenomegaly	Presence of bleeding
Presence of abdominal pain	Spearman's rho	-	0.01	-0.04	-0.01	0.14	-0.08	0.20	0.20	0.17
	p value		0.918	0.772	0.943	0.240	0.512	0.106	0.106	0.170
Presence of fever	Spearman's rho	0.01	-	0.11	0.08	0.21	0.10	-0.07	-0.07	0.00
	p value	0.918		0.359	0.489	0.087	0.408	0.559	0.559	0.980
Presence of bone pain	Spearman's rho	-0.04	0.11	-	0.05	0.02	-0.08	-0.16	-0.22	-0.04
	p value	0.772	0.359		0.697	0.889	0.517	0.182	0.068	0.763
CNS status	Spearman's rho	-0.01	0.08	0.05	-	0.02	0.08	-0.07	-0.07	-0.05
	p value	0.943	0.489	0.697		0.851	0.500	0.556	0.556	0.654
Presence of pallor	Spearman's rho	0.14	0.21	0.02	0.02	-	0.14	0.09	-0.11	0.09
	p value	0.240	0.087	0.889	0.851		0.243	0.470	0.385	0.467
Presence of anorexia	Spearman's rho	-0.08	0.10	-0.08	0.08	0.14	-	-0.04	0.13	0.11
	p value	0.512	0.408	0.517	0.500	0.243		0.760	0.270	0.373
Presence of hepatomegaly	Spearman's rho	0.20	-0.07	-0.16	-0.07	0.09	-0.04	-	0.77	0.04
	p value	0.106	0.559	0.182	0.556	0.470	0.760		0.000	0.727
Presence of splenomegaly	Spearman's rho	0.20	-0.07	-0.22	-0.07	-0.11	0.13	0.77	-	0.11
	p value	0.106	0.559	0.068	0.556	0.385	0.270	<0.001		0.355
Presence of bleeding	Spearman's rho	0.17	0.00	-0.04	-0.05	0.09	0.11	0.04	0.11	-
	p value	0.170	0.980	0.763	0.654	0.467	0.373	0.727	0.355	
Immunophenotype	Spearman's rho	0.04	0.11	0.22	-0.11	0.25	0.09	0.06	-0.01	0.00
	p value	0.770	0.373	0.064	0.379	0.035	0.470	0.597	0.952	0.975
Relapse	Spearman's rho	-0.07	-0.08	-0.13	0.06	-0.08	-0.11	0.17	0.06	-0.15
	p value	0.561	0.533	0.278	0.627	0.524	0.376	0.158	0.625	0.227

Discussion

This is the first description of hematological laboratory findings, signs and symptoms at presentation, immunophenotype, cytogenetics, and outcomes of induction chemotherapy for patients with pediatric ALL who received induction chemotherapy at the main referral hospital for pediatric ALL patients in Palestine. The study also established associations between hematological laboratory findings, sociodemographic, and clinical variables of the patients.

The median age at diagnosis in this study was 6.0 with an IQR of 3.5 years. This was comparable to what was reported in a previous large study on Middle Eastern Arab populations [7]. Findings of this study were also consistent with those reported among Saudi Arabians [30], Jordanians [31], and Brazilians [32]. In this study, patients with pediatric ALL were predominantly male in gender (60.9%). Findings of this study were consistent with those reported in a previous

larger study in the Middle East [7] and other regional studies in Saudi Arabia [30], Oman [33], and Pakistan [34]. Findings of other studies reported in Brazil were different with regard to the prevalence of pediatric ALL among male and female patients [32, 35].

At presentation, the median hemoglobin concentration was 9.0 with an IQR of 2.7 g/dL. Hemoglobin levels reported in this study were comparable to those reported in a previous larger study in the Middle East [7] and other regional studies in Jordan [31] and Brazil [32]. Hemoglobin levels differed significantly between children older and younger than 5 years and those who had T-ALL or B-ALL. Findings of this study were consistent with those reported in previous studies [10, 25]. The median platelet count was 80,000 with an IQR of 157000 platelets/mm³. In a previous larger study in the Middle East, the platelet count was 36,600 platelets/mm³ [7]. In this study, patients who had splenomegaly and those who had bleeding symptoms had significantly lower platelet count than patients without splenomegaly and bleeding symptoms. Platelet counts after induction chemotherapy could be useful in treatment stratification of patients with pediatric ALL [16, 17]. Platelet counts could also be used in predicting prognosis and response to chemotherapy [16, 20]. The median initial WBCs count was 7,100 with an IQR of 20,600 cells/mm³. The median initial WBCs counts were significantly different between patients who had T-ALL and B-ALL. Similarly, the absolute neutrophils counts were also significantly different between patients who had T-ALL and B-ALL. Our findings were consistent with the reported complete blood count and clinical findings of patients with pediatric ALL [10].

Pediatric ALL has many clinical manifestations and patients usually symptomatic at presentation. Usually, symptoms result from dysfunction of the different blood cells. In this study, pallor (72.5%), fever (53.6%), bone pain (43.5%), abdominal pain (31.9%) and bleeding symptoms (21.7%) were the main manifestations at presentation. Our findings showed that pallor was significantly associated with T-ALL. Presence of hepatomegaly was significantly associated with splenomegaly. Manifestations reported in this study were consistent with those reported in larger studies in the Middle East where fever (75.5%), bone pain (39.6%), and bleeding symptoms (30.8%) were the most frequent manifestations of pediatric ALL [7]. In Saudi Arabia, patients presented with fever (70%), bleeding symptoms (18%), and bone pain (10%) [30]. In this study, splenomegaly was reported in 49.3% of the patients. Al-Mulla et al reported that 60.8% of patients with pediatric ALL had splenomegaly [7]. Among Saudi Arabians with pediatric ALL, 42% of the patients had splenomegaly [30]. In Brazil, Lustosa de Sousa et al reported that 57.8% of the patients with pediatric ALL had splenomegaly [32]. Hepatomegaly was present in 49.3% of the patients with pediatric ALL included in this study. Findings of this study were consistent with those reported in the region among Arab populations in the Middle East and Saudi Arabia as well as those reported among Brazilians [7, 30, 32].

Consistent with international and regional studies, 79.7% of the patients had B-ALL and 20.3% of the patients had T-ALL. Findings of this study mirrored those reported in international studies as well as those reported in the Middle East and the region. B-ALL was prevalent in 85% of Middle Eastern patients with ALL [7], 82% of Saudi Arabian patients [30], and 89.5% of Brazilian patients [32].

Findings of this study reported that the vast majority of the patients (95.7%) had CNS status 1. Our findings were consistent with those reported among Middle Eastern, Saudi Arabian, Moroccan, and Brazilian patients with pediatric ALL [7, 30, 32, 36]. In this study, 1.4% and 2.9% of the patients had CNS status 2 and CNS status 2, respectively. Again, these results were comparable with those reported among Middle Eastern, Saudi Arabian, Moroccan, and Brazilian patients with pediatric ALL [7, 30, 32, 36].

Although cytogenetic studies were not conducted for all patients, findings of this study were consistent with those reported for the hyperdiploidy, t(12,21), t(1,19), and t(9,22) translocations among patients with pediatric ALL. For example, in a study conducted in King Hussein Center in Jordan reported that about 12% of the patients with pediatric ALL were positive for translocation (12,21), 1.7% were positive for translocation (1,19), and 7.4% were positive for translocation (9,22) [31]. Among Middle Eastern patients with pediatric ALL, 5.1% had (9,22) translocation [7]. In Chinese patients, 12.5% had (9,22), 8.3% had (1,19), and 41.6% did not have genetic abnormalities [37]. In contrast, another study conducted in Iran reported that hyperdiploidy was the most prevalent cytogenetic abnormality (32%) among patients with pediatric ALL [38].

After induction chemotherapy, the vast majority (98.5%) of the patients included in this study had complete remission. In a larger Middle Eastern study, remission rate was as high as 96.6% [7]. In Jordan, the remission rate was 7% [31]. In this study, 7.2% of the patients who showed complete remission developed relapse. Relapse rates after complete remission showed variability in previously reported studies in Jordan (9%) and Pakistan (20%) [31, 34].

Strengths and limitations

Findings of this study might be interpreted after carefully considering the following strengths and limitations. First, this investigation is the first to describe clinical characteristics and outcomes of patients with pediatric ALL in Palestine. Palestinian patients were not included in previous large studies in the Middle East [7]. Second, correlations between sociodemographic and clinical characteristics of the patients were also included in the descriptive approach followed in this study. Third, this study was based on data collected from the medical record of the patients. Although a data collection form was specifically designed for this study and field researchers had access to the records as many times as they needed, the data collected could be biased by incorrectly entered information in the medical records. Fourth, this was a single-center study. Although An-Najah National Hospital has emerged as the main referral center for patients with leukemia, including those with pediatric ALL in the West Bank and Gaza Strip, inclusion of other centers could have permitted complete description of patients with pediatric ALL in Palestine. Fifth, the sample size included in this study was relatively small. This could be attributed to the fact that care for patients with cancer is based on fragmentation and patients often receive healthcare outside Palestine. Finally, determining more accurate relapse needs longer time as patients need to be followed for 2-3 years after complete remission to decide if a patient developed relapse or not.

Conclusion

Overall, this study provides insights into the clinical characteristics and outcomes of induction chemotherapy in Palestinian patients with pediatric ALL. The characteristics of ALL among Palestinians were comparable to their peers in the region. The outcomes of induction chemotherapy were also comparable to other published data for ALL patients. More studies are still needed to determine the cytogenetics and relapse rates after induction of chemotherapy.

Abbreviations

ALL: Acute lymphoblastic leukemia

B-ALL: B-cell precursor immunophenotype-acute lymphoblastic leukemia

CNS: Central nervous system

IQR: Interquartile range

IRB: Institutional Review Board

MECCA: Middle East Childhood Cancer Alliance

T-ALL: T-cell precursor immunophenotype-acute lymphoblastic leukemia

WBC: White blood cell

WHO: World Health Organization

Declarations

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request for privacy reasons.

Supplementary information

The data collection for is shown in Additional file 1.

Additional Table S1. The data collection form

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Authors' contributions

RS and SM conceived and designed the study. SM, YO, RH, and MA collected the data. RS, SM, YO, RH, and MA contributed to data analysis. RS interpreted the data. RS, SM, YO, RH, and MA drafted the manuscript. RS critically revised the manuscript. All authors approved the final manuscript.

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Ethics approval and consent to participate

The protocol and ethics of this study were approved by the Institutional Review Board (IRB) of An-Najah National University under the archived number (IRB-20-2017). Data and information leading to the identity of the patient were not collected into the data collection form. The data were coded during the data analysis.

Consent for publication

Not applicable.

Competing interests

The author declare that they have no competing interests.

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