Clinical characteristics and outcomes of patients with pediatric acute lymphoblastic leukemia after induction of chemotherapy: a pilot descriptive correlational study from Palestine

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Abstract

Objective: 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.

Results: Complete data of 69 patients were included in this analysis. The majority (79.7%) of the patients had B-ALL phenotype. After induction chemotherapy, remission was experienced by the vast majority of the patients and 5 (7.2%) experienced relapses. 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 in 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 palmar pollar was positively associated (p value = 0.035) with T-cell ALL. Presence of hepatomegaly was positively associated (p value < 0.001) with splenomegaly.

Keywords: Acute lymphoblastic leukemia, Induction chemotherapy, Treatment, Translocation, Palestine

Introduction

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 type of cancer 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 population 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. On annual basis, about 6000 ALL cases are diagnosed in the US, of those, about 50% are children and teenagers [4, 5].

In Palestine, cancer care is highly fragmented and a high percentage of patients receive treatment outside the country [1, 6]. Currently, referral hospitals in which patients with pediatric ALL receive induction chemotherapy in Palestine are limited [1, 6]. Since its inception, An-Najah National Hospital has emerged as the...
main referral hospital for pediatric ALL in Palestine. Description of the epidemiological and clinical characteristics of patients with ALL in different nations has received considerable attention [7]. The Middle East Childhood Cancer Alliance (MECCA) collected clinical and demographic data on children with ALL from 16 countries in the Middle East [8]. However, Palestinians were not included in MECCA’s study. Currently, little is known on the epidemiological and clinical characteristics of patients with pediatric ALL among Palestinians [2]. Therefore, this pilot 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 the associations between sociodemographic and clinical characteristics of the patients included in the study. The study provided insights into the clinical characteristics and outcomes of induction chemotherapy in Palestinian patients with pediatric ALL.

Methods

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. With not restrict inclusion based on gender or admission dates. We excluded patients whose medical records were incomplete and those who received their induction chemotherapy outside the referral hospital. All patients with a diagnosis of pediatric ALL regardless of their gender or admission dates were screened against the inclusion and exclusion criteria.

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 relevant to sociodemographic, physical examination, daily progress, hematological, clinical, bone marrow biopsies, flow cytometry, and cytogenetics. The data collected for this study were informed by previous studies [8–10]. 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 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% blast on bone marrow), (b) non-remission (≥5% blast on bone marrow), (c) relapse (≥20% blast in bone marrow, any blasts in CNS or both, or (d) death of the patient during the first admission for the induction chemotherapy.

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 correlation. 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, clinical, and hematological variables of the study patients

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. Detailed sociodemographic, clinical, and hematological variables of the patients are shown in Table 1.

Association between the different sociodemographic and clinical variables 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) (Table 2). 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 (5000 with an IQR of 10,950). The median absolute neutrophil count for patients who had T-ALL (2670 with an IQR of 4595) was significantly higher (p value = 0.011) than those who had B-ALL (1050 with an IQR of 1730).

Correlation between sociodemographic and clinical characteristics of patients with pediatric ALL

There was a positive correlation (p value = 0.035) between the presence of pallor at presentation and T-ALL immunophenotype. Again, there was a positive correlation (p value < 0.001) between the presence of hepatomegaly and the presence of splenomegaly (Table 3).

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.

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 [8] and other regional studies in Jordan [11] and Brazil.
| Variable                  | n  | %   | Median | IQR   | Mean rank | P value | Median | IQR   | Mean rank | P value | Median | IQR   | Mean rank | P value |
|--------------------------|----|-----|--------|-------|-----------|---------|--------|-------|-----------|---------|--------|-------|-----------|---------|
| Age (years)              |    |     |        |       |           |         |        |       |           |         |        |       |           |         |
| < 10                     | 26 | 37.7| 7.8    | 28.2  | 26.6      | 0.007   | 57000  | 93000 | 30.2      | 0.119   | 7700   | 26400 | 37.3      | 0.454   |
| ≥ 10                     | 43 | 62.3| 9.1    | 25.0  | 40.1      |         | 118500 | 167000| 37.9      |         | 4600   | 11028 | 33.6      |         |
| Gender                   |    |     |        |       |           |         |        |       |           |         |        |       |           |         |
| Male                     | 42 | 60.9| 8.5    | 30.6  | 38.3      | 0.088   | 87000  | 162500| 36.1      | 0.563   | 7100   | 18700 | 38.4      | 0.077   |
| Female                   | 27 | 39.1| 9.0    | 36.2  | 29.9      |         | 67000  | 171000| 33.3      |         | 5000   | 7550  | 29.7      |         |
| Presence of abdominal pain |    |     |        |       |           |         |        |       |           |         |        |       |           |         |
| Yes                      | 22 | 31.9| 9.0    | 35.4  | 34.2      | 0.822   | 88500  | 179000| 35.6      | 0.867   | 5100   | 10670 | 36.4      | 0.690   |
| No                       | 47 | 68.1| 8.8    | 30.6  | 35.4      |         | 64000  | 167000| 34.7      |         | 7100   | 16700 | 34.3      |         |
| Presence of fever        |    |     |        |       |           |         |        |       |           |         |        |       |           |         |
| Yes                      | 37 | 53.6| 9.0    | 26.7  | 37.8      | 0.217   | 78000  | 155250| 34.7      | 0.909   | 4900   | 17178 | 34.8      | 0.942   |
| No                       | 32 | 46.4| 8.5    | 25.3  | 31.8      |         | 64000  | 180500| 35.3      |         | 7700   | 13950 | 35.2      |         |
| Presence of bone pain    |    |     |        |       |           |         |        |       |           |         |        |       |           |         |
| Yes                      | 30 | 43.5| 9.1    | 29.5  | 34.8      | 0.928   | 59000  | 123000| 33.2      | 0.506   | 5300   | 13100 | 33.4      | 0.553   |
| No                       | 39 | 56.5| 8.7    | 22.5  | 35.2      |         | 88500  | 185500| 36.4      |         | 5650   | 16725 | 36.3      |         |
| Pallor                   |    |     |        |       |           |         |        |       |           |         |        |       |           |         |
| Yes                      | 50 | 72.5| 8.5    | 28.5  | 32.6      | 0.111   | 84000  | 157000| 35.9      | 0.537   | 5300   | 13970 | 34.0      | 0.515   |
| No                       | 19 | 27.5| 9.4    | 3.5   | 41.2      |         | 65500  | 211800| 32.6      |         | 7300   | 19750 | 37.6      |         |
| Presence of anorexia     |    |     |        |       |           |         |        |       |           |         |        |       |           |         |
| Yes                      | 9  | 13.0| 8.3    | 26.2  | 30.3      | 0.449   | 121000 | 168000| 37.3      | 0.708   | 17700  | 32350 | 40.8      | 0.354   |
| No                       | 60 | 87.0| 9.0    | 25.7  | 35.7      |         | 71000  | 158000| 34.7      |         | 5000   | 12643 | 34.1      |         |
| 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   |
| No                       | 35 | 50.7| 8.3    | 3.8   | 33.9      |         | 118500 | 173000| 38.4      |         | 6350   | 14350 | 33.4      |         |
| 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   |
| No                       | 35 | 50.7| 7.8    | 3.0   | 32.9      |         | 122000 | 169000| 41.0      |         | 5200   | 9250  | 32.1      |         |
| Presence of bleeding     |    |     |        |       |           |         |        |       |           |         |        |       |           |         |
| Yes                      | 15 | 21.7| 8.0    | 4.3   | 30.6      | 0.333   | 34000  | 66050  | 22.9      | 0.008   | 9600   | 12335 | 39.1      | 0.367   |
| No                       | 54 | 78.3| 8.9    | 2.2   | 36.2      |         | 103000 | 171000| 38.4      |         | 4900   | 15300 | 33.9      |         |
| 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  |
| T-cell ALL               | 14 | 20.3| 11.2   | 2.8   | 54.6      |         | 97500  | 264600| 37.9      |         | 22100  | 35550 | 52.3      |         |
Table 2 (continued)

| Variable  | n  | %  | Median | IQR | Mean rank | P value | Median | IQR | Mean rank | P value | Median | IQR | Mean rank | P value |
|-----------|----|----|--------|-----|-----------|---------|--------|-----|-----------|---------|--------|-----|-----------|---------|
| Relapse   |    |    |        |     |           |         |        |     |           |         |        |     |           |         |
| Yes       | 5  | 7.2| 7.8000 | 1.35| 31.8      | 0.711   | 60500  | 166750| 38.2       | 0.711   | 1290   | 2353| 24.7      | 0.233   |
| No        | 64 | 92.8| 9.0000 | 2.80| 35.3      |          | 84000  | 166000| 34.8       |          | 5600   | 14500| 35.8      |          |

Hemoglobin (g/dL)  Platelet count  Initial WBC count  Absolute neutrophil count
| Variable                      | 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 | Immunophenotype | Relapse |
|-------------------------------|-------------|-----------------------------|------------------|-----------------------|------------|--------------------|----------------------|------------------------|------------------------|----------------------|-------------------|---------|
| Presence of abdominal pain    | Spearman's rho | –                            | 0.01             | –                     | 0.04       | –                  | 0.01                 | 0.20                   | 0.20                   | 0.17                 | 0.04              | – 0.07  |
| p value                       |             | 0.918                        | 0.772            | 0.943                 | 0.724      | 0.240              | 0.512               | 0.106                  | 0.106                  | 0.170               | 0.770             | 0.561   |
| Presence of fever             | Spearman's rho | 0.001                        | –                | 0.11                  | 0.08       | 0.21               | 0.10                | –0.07                  | –0.07                  | 0.00                 | 0.11              | – 0.08  |
| p value                       |             | 0.918                        | 0.359            | 0.489                 | 0.240      | 0.087              | 0.408               | 0.559                  | 0.559                  | 0.170               | 0.770             | 0.533   |
| Presence of bone pain         | Spearman's rho | –0.04                        | 0.01             | –                     | 0.05       | 0.02               | –0.08               | –0.16                  | –0.22                  | –0.04               | 0.22              | – 0.13  |
| p value                       |             | 0.772                        | 0.359            | 0.697                 | 0.889      | 0.517              | 0.182               | 0.068                  | 0.763                  | 0.064               | 0.278             |         |
| CNS status                    | Spearman's rho | –0.01                        | 0.08             | 0.05                  | 0.02       | 0.08               | –0.07               | –0.07                  | –0.05                  | –0.11               | 0.06              | –       |
| p value                       |             | 0.943                        | 0.489            | 0.697                 | 0.851      | 0.500              | 0.556               | 0.556                  | 0.654                  | 0.379               | 0.627             |         |
| Presence of pallor            | Spearman's rho | 0.14                         | 0.21             | 0.02                  | 0.02       | –                  | 0.14                | 0.09                   | –0.11                  | 0.09                | 0.25              | – 0.08  |
| p value                       |             | 0.240                        | 0.087            | 0.889                 | 0.851      | 0.243              | 0.470               | 0.385                  | 0.467                  | 0.035               | 0.524             |         |
| Presence of anorexia          | Spearman's rho | –0.08                        | 0.10             | –0.08                 | 0.08      | 0.14               | –                   | –0.04                  | 0.13                   | 0.11                | 0.09              | – 0.11  |
| p value                       |             | 0.512                        | 0.408            | 0.517                 | 0.500      | 0.243              | 0.760               | 0.270                  | 0.037                  | 0.470               | 0.376             |         |
| Presence of hepatomegaly      | Spearman's rho | 0.20                         | –0.07            | –0.16                 | –0.07     | 0.09               | –0.04               | –                      | 0.77                   | 0.04                | 0.06              | 0.17    |
| p value                       |             | 0.20                         | 0.559            | 0.182                 | 0.556     | 0.470              | 0.760               | <0.001                 | 0.072                  | 0.597               | 0.158             |         |
| Presence of splenomegaly      | Spearman's rho | 0.020                        | –0.07            | –0.22                 | –0.07     | –0.11              | 0.13                | 0.77                   | –                      | 0.11                | –0.01             | 0.06    |
| p value                       |             | 0.010                        | 0.559            | 0.068                 | 0.556     | 0.385              | 0.270               | <0.001                 | 0.035                  | 0.952               | 0.625             |         |
| Presence of bleeding          | Spearman's rho | 0.017                        | 0.00             | –0.04                 | –0.05     | 0.11               | 0.09                | 0.04                   | 0.11                   | –0.01              | 0.00              | – 0.15  |
| p value                       |             | 0.17                         | 0.980            | 0.763                 | 0.654     | 0.467              | 0.373               | 0.727                  | 0.355                  | 0.097               | 0.227             |         |
| Immunophenotype              | Spearman's rho | 0.004                        | 0.011            | 0.22                  | –0.11     | 0.25               | 0.09                | 0.06                   | –0.01                  | 0.00                | –0.00             |         |
| p value                       |             | 0.770                        | 0.373            | 0.064                 | 0.379     | 0.035              | 0.470               | 0.597                  | 0.952                  | 0.975               | 0.987             |         |
| Relapse                       | Spearman's rho | –0.07                        | –0.08            | –0.13                 | –0.08     | –0.11              | 0.17                | 0.06                   | –0.15                  | 0.00                | –                 |         |
| p value                       |             | 0.561                        | 0.533            | 0.278                 | 0.627     | 0.524              | 0.376               | 0.158                  | 0.625                  | 0.227               | 0.987             |         |
Finding of this study reported that the vast majority of the patients (95.7%) had CNS status 1. Previous studies have shown that CNS infiltration altered protein profiling of the CSF [18]. Our findings were consistent with those reported among Middle Eastern, Saudi Arabian, Moroccan, and Brazilian patients with pediatric ALL [8, 10, 12, 19]. Although cytogenetic studies were not conducted for all patients, the 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 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) [11]. Among Middle Eastern patients with pediatric ALL, 5.1% had (9, 22) translocation [8]. After induction chemotherapy, the vast majority (98.5%) of the patients included in this study had complete remission. In a larger Middle Eastern study, the remission rate was as high as 96.6% [8]. In Jordan, the remission rate was 7% [11]. 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%) [11, 20].

**Limitations**

First, 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. Second, 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, the inclusion of other centers could have permitted a complete description of patients with pediatric ALL in Palestine. Third, 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.

**Abbreviations**

ALL: Acute lymphoblastic leukemia; B-ALL: B-cell precursor immunophenotype-acute lymphoblastic leukemia; CNS: Central nervous system; IQR: Inter-quartile 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.
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Authors’ contributions

RS and SM were involved in the conception and design of the work, analysis and interpretation of data, drafting and final approval the manuscript. YO, RH, and MA were involved in the data acquisition, analysis, drafting the work and final approval of the version to be published. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

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). Approval was also obtained from the hospital administration to access the patient information. 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

All authors declare that they have no competing interest.

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