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Research Article

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Survival and outcome of acute lymphoblastic leukemia in Children Attending Leukemia Center in Al- Kuwait University Hospital in Sana'a, Yemen

Mohammed Abduh Aqlan[1*], Nawal Al-Mughales[2], Abdulrahman Alhadi[3] and Ali Al-Zaazaai[4*]

[1]Assistant Professor in Faculty of Medicine – 21_September university, Consultant in Pediatrics, University hospital , Sana'a - Yemen

[2]Assistant Professor in Faculty of Medicine - 21_September university, Consultant in Pediatrics, University hospital , Sana'a - Yemen

[3]Professor of Pediatrics and Pediatric Hematology -Oncology Faculty of Medicine-Sana'a University Member of Scientific Council of Pediatrics, Coordinator of Pediatrics Specialty in Yemen

[4]M.Sc. Clinical Pharmacy of Wenzhou Medical University, Zhejiang Province, China

[*]Corresponding author

Dr. Mohammed Abduh Ali Aqlan, Assistant Professor in Faculty of Medicine – 21_September university, Consultant in Pediatrics, University hospital, Member of Scientific Council of Pediatrics, Yemen.

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ABSTRACT

Background: Acute leukemia is the most common cancer seen in children in Yemen. Leukemia represents the 11th and 10th most frequent cause of cancer morbidity and mortality worldwide, respectively. The survival of patients with acute lymphoblastic leukemia (ALL) has improved significantly with the use of intensive multimodality treatment regimens. There are advances have been made in the treatment of acute lymphoblastic leukemia with 5-year overall survival rate reaching 90% in the high-income countries.

Objective: To determine the five years survival and outcome of children with acute lymphoblastic leukemia (ALL) admitted to leukemia center in Al-Kuwait university Hospital in Sana'a, during the period from January 2011 to January 2015.

Methods and patients: A cross-sectional retrospective study which relied on reviewing data available in patients' records in leukemia center. A checklist was prepared for data collection which included demographic data, WBC counts, remission of ALL, relapse cases, 5 years survival, outcome and causes of death. SPSS software was used for data analysis.

Results: This study included 171 children of ALL. Males represented the majority in a rate of 69.1 %. Most cases (about 46.2%) were in the age group from 1 to 5 years, and 31 % were in age group between 6 to 10 years. Most cases (85%) of children are with total WBC less than 50000. Most of children (about 83.6 %) develop complete bone marrow remission at day of 22 of start chemotherapy. There is 72.2 % of known cases survive more than 5 years from date of diagnosis while 57.7 % of known cases survive more than 5 years after finish chemotherapy. Children with relapse of acute lymphoblastic leukemia were 27 %. The rate of cure of acute lymphoblastic leukemia in pediatric patients was 45 % and the patients discharged against medical advice (DAMA) were 8.8 % while 24 % of cases were died, and there were 2.3 % relapsed cases. On other hand there were 19.9 % of cases lost during follow-up. The most cases of death died during chemotherapy 73%, then 15% died before starting chemotherapy, and 12% died after complete chemotherapy period. The infection was most common cause of death 51.2 %.

Conclusions: About half of cases of acute lymphoblastic leukemia were in the age group from 1 to 5 years. Most of children with acute lymphoblastic leukemia develop complete bone marrow remission at day of 22 (about 83.6 %).

There is two third of known cases of acute lymphoblastic leukemia survive more than 5 years from date of diagnosis and about one fourth of all cases relapsed. About half cases of acute lymphoblastic leukemia in pediatric patients were cured, while less than fourth of all cases died and more than half of dead cases died due to infection.

The outcomes of acute lymphoblastic leukemia continue to improve with more long-term survivors, decrease complications and treatment side effects should become a major focus. Future research could focus on identifying factors affecting the outcome and causes of death among children with leukemia.

Keywords: Acute Lymphoblastic Leukemia, Remission, Survival, Outcome, Chemotherapy, Death

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List of Abbreviation

ALL	**Acute lymphoid leukemia**
AML	**Acute myeloid leukemia**
CLL	**Chronic lymphoid leukemia**
CML	**Chronic myeloid leukemia**
CNS	**Central nervous system**
DAMA	**Discharged against medical advice**
JMML	**Juvenile myelomonocytic leukemia**
SPSS	**Statistical Package for the Social Sciences**

Chapter 1: Introduction

Background

Acute leukemia is one of the most common types of cancers among children [1]. Leukemia is the most common cancer seen in children including Yemen [2,3]. Leukemia caused about 265,471 deaths worldwide in 2012 [4]. Leukemia is the eleventh and tenth most common cause of cancer morbidity and mortality worldwide, respectively [5]. Leukemia is a malignancy that arises from proliferation of hematopoietic cells leading to disruption of normal marrow function and marrow failure. The clinical manifestations of leukemia are result of the unregulated proliferation of the malignant clone and bone marrow failure [6].

In Europe, there were 46,449 males and 35,880 female children diagnosed with leukemia in 2012. About 233,451 populations were diagnosed with leukemia in Australia, Asia, and the USA by 2017. In contrast, it has an incidence of 23,928 cases (ASR 3.0 per 100,000) in Africa by 2012 [7,8].

There are two main subtypes of acute leukemias in children; the commoner acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). Acute lymphocytic leukemia (ALL) is a malignant transformation and proliferation of lymphoid progenitor cells in the bone marrow, blood and extramedullary sites; While 80% of ALL occurs in children, it represents a devastating disease when it occurs in adults. Within the United States, the incidence of ALL is estimated at 1.6 per 100 000 populations. In 2016 alone, an estimated 6590 new cases were diagnosed, with over 1400 deaths due to ALL (American Cancer Society). The incidence of ALL follows a bimodal distribution, with the first peak occurring in childhood and a second peak occurring around the age of 50 [9].

Despite its high fatality rate, less attention has been paid to the problem in developing countries, including Yemen [10]. According to study conducted in Hadramout, leukemia represented the most common childhood cancer in a rate of 25.2% [5]. Reports from different countries found that in children under 15 years of age, the leukemia is the commonest type of tumor [6,11, 12].

The survival of patients with acute lymphoblastic leukemia (ALL) has improved significantly with the use of intensive multimodality treatment regimens.

Remarkable progress has been made in the treatment of acute lymphoblastic leukemia (ALL, which constitute 75-80% of childhood acute leukemias) with 5-year overall survival rate reaching 90% in the high-income countries [13].

According to the Limited Yemen leukemia Studies, the most common cancer among Yemeni children and adults were leukemia (33.1%), lymphoma (31.5%) [14,15].

This study aimed at determining the outcome and five years survival among leukemic children attending leukemia center in Al- Kuwait university Hospital in Sana'a that the only center specialized of this disease in Yemen.

Objectives of the study

A: General objective

To determine five years survival rate and outcome of children with acute lymphoblastic leukemia admitted in leukemia center in Al-Kuwait university hospital in Sana'a during period from January 2011 to January 2015.

B: Specific Objectives

1. To explore demographic characteristics (age, gender) for children with acute lymphoblastic leukemia.
2. To determine some risk factors of acute lymphoblastic leukemia in children admitted in leukemia center in Al-Kuwait university hospital in Sana'a.
3. To determine percentage of remission of acute lymphoblastic leukemia in children admitted in leukemia center in Al-Kuwait university hospital in Sana'a.
4. To determine outcomes of children with leukemia admitted in leukemia center in Al-Kuwait university hospital in Sana'a.
5. To determine five years survival rate of children with leukemia from time of diagnosis and after finish chemotherapy admitted in leukemia center in Al-Kuwait university hospital in Sana'a.
6. To determine causes and time of death of children with acute lymphoblastic leukemia admitted in leukemia center in Al-Kuwait university hospital in Sana'a.

Chapter 2: Pateints and Methods

1. **Study design**
   Cross - sectional, descriptive study.
2. **Study place**
   The study has been conducted in the leukemia center in Al-Kuwait university hospital.
3. **Study population**
   Children under 18 years in age with acute lymphoblastic leukemia from January 2011 to January 2015 were included in this study
4. **Study period**
   All children with acute lymphoblastic leukemia admitted in leukemia center from January 2011 to January 2015 were included in this study and followed till January 2023.
5. **Inclusion criteria**
   All children with acute lymphoblastic leukemia, of both genders, encountered during the period of data collection were included in this study.
6. **Exclusion criteria**
   Cases of incomplete demographic or clinical data were excluded.
7. **Sampling method**
   A convenient sample was considered; no special technic was applied to choose cases.

8. **Study Tool and data collection**
   Data had been collected by the researcher. Over a period of study, patients records had been reviewed for relevant data. A questionnaire was used for the purpose of data collection. It included demographic data, data related to leukemia subtypes, initial WBC counts, bone marrow remission, poor prognostic factors, five years survival, outcome, time and cause of death.
9. **Data Analysis**
   Statistical Package for the Social Sciences (SPSS) software, version 23 was used for data analysis. Nominal and categorical variables were described by frequencies and percentages. Continuous variables were described by means & SD, minimum and maximum. Tables and graphs were used for data display.

Chi square test was applied to find association between variables. The test was considered to be significant if p value < 0.05.

Chapter 3: Results

Distribution of the patients according to gender:

Out of 171 children in the sample, males represented the majority of cases (113 = 66.1 %), and females accounted for (58 = 33.9 %), with male to female's ratio 1.9: 1.

Table 1: Distribution of the patients according to gender

Gender	Count	Percent
Males	113	66.1 %
Females	58	33.9 %
Total	171	100 %

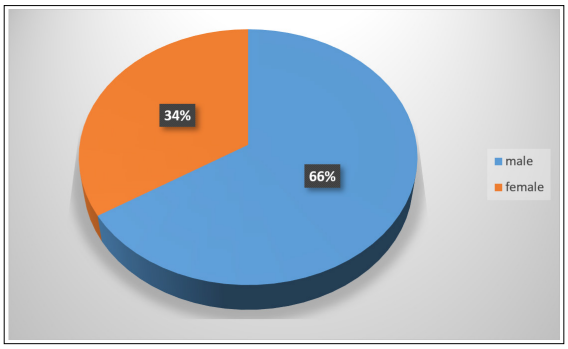

Figure 1: Distribution of the studied cases according to the gender

Distribution of the children with acute lymphoblastic leukemia according to age:

Most cases (about 46.2%) were in the age group from 1 to 5 years, then (31 %) were in age group between 6 to 10 years. Those more than 10 years represented (19.9 %), and those under 1 year represented only 2.9 %.

Table 2: Distribution of the children with acute lymphoblastic leukemia according to age

Age categories	Count	Percent %
Less than 1 year	5	2.9
1- 5 years	79	46.2
6 - 10 years	53	31
More than 10 years	34	19.9
Total	171	100

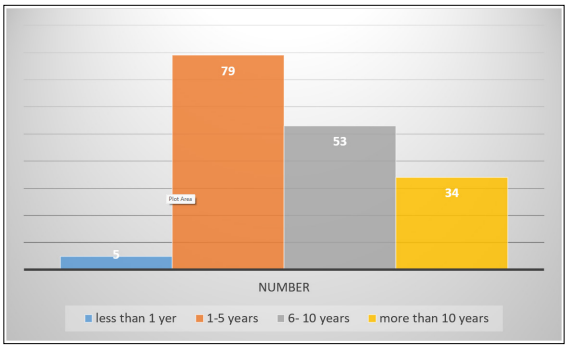

Figure 2: Distribution of the children with acute lymphoblastic leukemia according to age.

Distribution of the children with acute lymphoblastic leukemia according to initial WBC counts:

Most of children are with total WBC less than 50000 (about 85%). Only the minority (about 15%) of them are with total WBC more than 50000.

Table 3: Distribution of the children with acute lymphoblastic leukemia according to initial WBC counts:

WBC counts	Frequency	Percent %
Less than 50000	146	85.4
More than 50000	25	14.6
Total	171	100

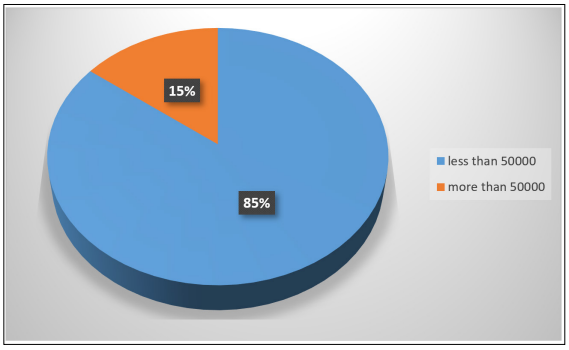

Figure 3: Initial WBC number of patients with acute lymphoblastic leukemia

Distribution of children according to complete remission at day of 22 of start chemotherapy:

Most of children develop complete bone marrow remission (about 83.6 %). Only the minority (14.6 %) of them are not develop remission by bone marrow remission and 1.8 % of children are unknown.

Table 4: Distribution of the children with acute lymphoblastic leukemia according to complete remission at day of 22 of start chemotherapy:

Status of remission	Frequency	Percent %
Complete remission	143	83.6
No remission	25	14.6
Unknown	3	1.8
Total	171	100

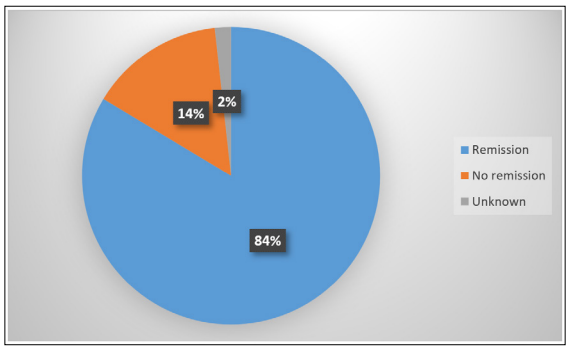

Figure 4: Distribution of the children with acute lymphoblastic leukemia according to complete remission at day of 22 of start chemotherapy

Percentage of pediatric leukemia patients with more than five years survival from time of diagnosis:
Most of children are survive more than 5 years were (56.1 %), and children that survive less than 5 years were (21.6%). There are (22.2 %) of them are unknown. Therefore, of known cases there is 72.2 % of cases survive more than 5 years from date of diagnosis (Figure 5).

Table 5: Five years survival of children with acute lymphoblastic leukemia

Status of remission	Frequency	Percent %
More than 5 years survival	96	56.1
Less than 5 years survival	37	21.6
Unknown	38	22.2
Total	171	100

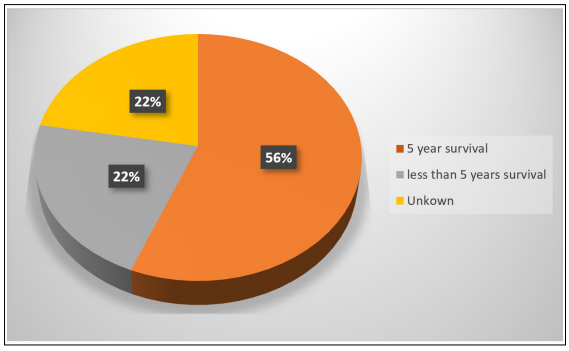

Figure 5: Five years survival of children with acute lymphoblastic leukemia

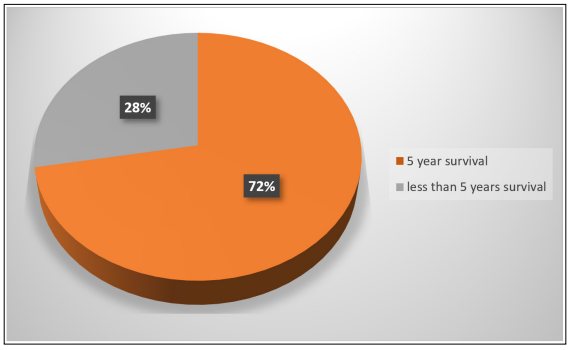

Figure 6: Five years survival of children with acute lymphoblastic leukemia (only known cases)

Percentage of survival of pediatric patients with acute lymphocytic more than five years after finish chemotherapy:
Many of children were survive more than 5 years after finish chemotherapy (41.5 %), and children that survived less than 5 years after finish chemotherapy were (25.1%) and there were 5.3% of cases did not complete 5 years after finish chemotherapy. The reminder of cases was unknown (28.1 %). Therefore, of known cases there is 57.7 % of cases survive more than 5 years after finish chemotherapy (Figure 6).

Table 6: Five years survival of children with acute lymphoblastic leukemia after finish chemotherapy

Status of remission	Frequency	Percent %
More than 5 years survival after finish chemotherapy	71	41.5
Less than 5 years survival after finish chemotherapy	43	25.1
Not finish 5 years of chemotherapy	9	5.3
Unknown	48	28.1
Total	171	100

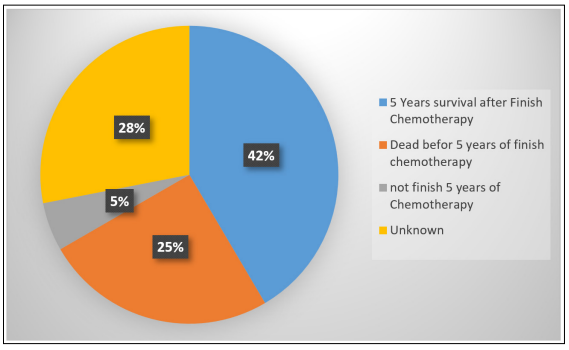

Figure 7: Percentage of five years survival of pediatric patients with acute lymphoblastic leukemia after finish chemotherapy

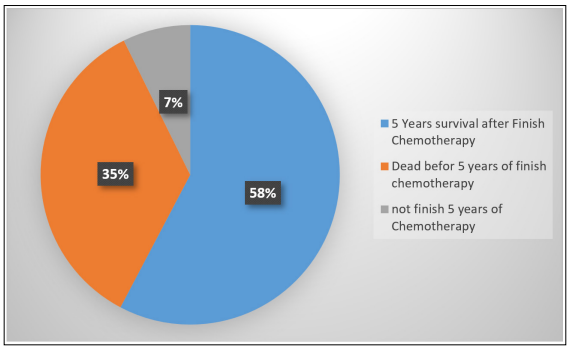

Figure 8: Percentage of five years survival of pediatric patients with acute lymphoblastic leukemia after finish chemotherapy (known cases)

Distribution of poor prognostic factors affecting the outcome in the children with acute lymphoblastic leukemia:
Children with relapse of acute lymphoblastic leukemia were 27 %, and those with failure of treatment represent 3.5 %. Central nervous system leukemia at presentation represent 1.8 %, and those with family history of acute lymphoblastic leukemia represent 1.8 %. The remaining portion 80.1% were with no known risk factors.

Table 7: Distribution of poor prognostic factors affecting the outcome in the children with acute lymphoblastic leukemia:

Poor prognostic factors affecting the outcome	Frequency	Percent %
Relapse	27	15.8
failure of treatment	6	3.5
Central nervous system leukemia at presentation	3	1.8
Positive family history	3	1.8

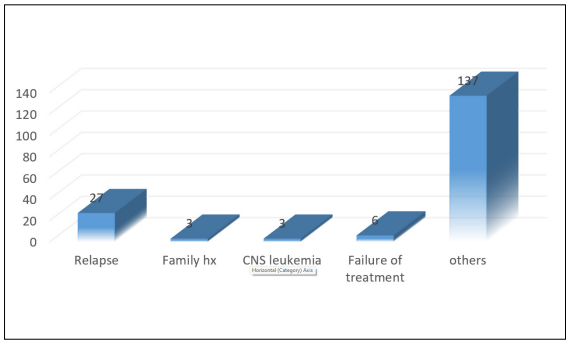

Figure 9: Distribution of poor prognostic factors affecting the outcome in the children with acute lymphoblastic leukemia

Outcome of the children with acute lymphoblastic leukemia: The table 3.8 shows the rate of cure of acute lymphoblastic leukemia in pediatric patients was 45 % and the patients discharged against medical advice (DAMA) were 8.8 % while 24 % of cases were died, and there were 2.3 % relapsed cases. On other hand there were 19.9 % of cases lost during follow-up.

Table 8: Distribution of outcome of the children with acute lymphoblastic leukemia

The outcome of acute lymphoblastic leukemia	Frequency	Percent %
Cured	77	45
DAMA	15	8.8
Dead	41	24
Relapse	4	2.3
Lost cases	34	19.9
Total	171	100

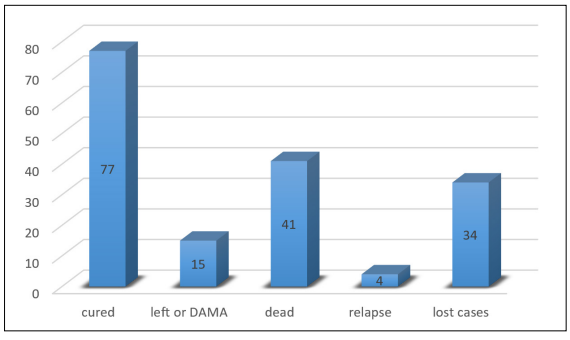

Figure 10: Outcome of the children with acute lymphoblastic leukemia

Relation the time of death to chemotherapy: Figure 10 show that the most cases of death died during chemotherapy 73%, then 15% died before starting chemotherapy, and 12% died after complete chemotherapy period.

Table 9: Distribution of death cases according to chemotherapy administrations

Relation of death to chemotherapy:	Frequency	Percent %
Died before starting chemotherapy	6	15
Died during chemotherapy	30	73
Died after complete chemotherapy period	5	12
Total	41	100

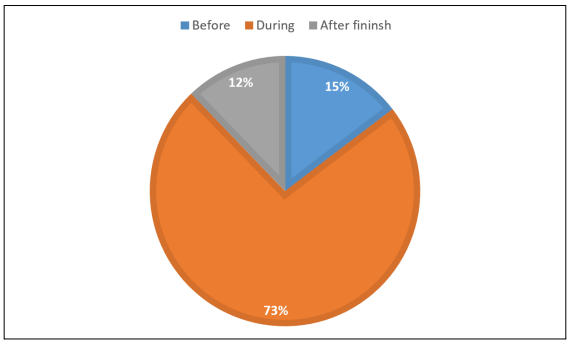

Figure 11: Relation the time of death to chemotherapy

Causes of death in acute lymphoblastic leukemia in children: Figure 11 shows the causes of death of children with acute lymphoblastic leukemia. It shows that sepsis or infection was most common cause of death 51.2 % of the cases followed by combination of sepsis and bleeding by 31.7 %, then bleeding only with 12.2 %. Leukocytosis, stroke and others were less than 5 %.

Table 10: Causes of death in acute lymphoblastic leukemia in children

Cause of death	Frequency	Percent %
Sepsis/ Infection	21	51.2
Sepsis and bleeding	13	31.7
Bleeding only	5	12.2
Others	2	4.9
Total	41	100

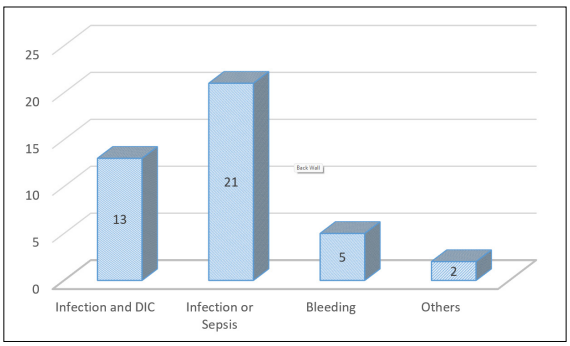

Figure 12: Causes of death in acute lymphoblastic leukemia in children

Chapter 4: Discussion

Despite the more advances in the treatment of pediatric leukemia, leukemia is still one of the most common causes of childhood deaths [16].

This study aimed at determining the survival and outcome of acute lymphoblastic leukemia children attending leukemia center in Al- Kuwait University Hospital in Sana'a. It has included 171 children diagnosed with acute lymphoblastic leukemia.

Males represented the majority in a rate of 66.1 %, which is in agreement with findings by Alhadi et al who found that males were predominant (66.7%) [10]. It is also consistent with a study by Ruqia Al-Barzinji in Iraq where 66.6% of patients were males [17]. In a study conducted by Aslam et al in India 58% of cases were males [18]. Said et al, in a study among Egyptian children observed that males represented 52.9% [19]. Similarly, Arico et al found that 55% of leukemic children were males [20]. There is no explanation for male gender predilection in leukemia.

Most cases of study (46.2%) were in the age group from 1 year to 5 years. Those between 6 years and 10 years represented 31%, and those above 10 years represented 19.9% , while cases below 1 year were only 2.9 % .This result is consistent with a study by Alhadi et al who found that the most of the cases (50%) were in the age group 1-5 years [10]. Said et al reported a range of age between 1.5 and 15 years with a mean of 8.0±3.9 years [19]. Findings are different with Arico et al who found that cases were ranged between 2.5 and 21.1 years [20].

The percentage of patients within WBC ≥ 50,000 µl in the present study (14.6 %) was lower than other studies. In study of Gaynon, et al it was 21% and in study of Schrappe et al was 19% [21,22].

Most of cases develop complete bone marrow remission (83.6 %) at day of 22 of start chemotherapy. Al-Shehab et al reported a remission rate of 94.2% which is slightly higher than remission rate found in our study [1].

Central nervous system involvement in the present study was only 1.8 % of patients, compared with 2.4-5.3% in western studies [21,22].

The relapse is one of the main predicting factors in ALL. The percent of patients with relapse was 15.8%, which is much less comparable to the study in Shiraz, Iran, with 34.1 % [23]. This percent is in the 23.4-41.1 range in many developing countries (23,24,28,29), In Turkey, this rate was 19.7%, which was comparable with Moricke et al.' study in which this percent was 16.2% [24,25].

In the last years, the survival rate of children diagnosed with ALL increased dramatically [21]. In the present study, similar to Zareifar et al. in Shiraz , the survival rate of ALL patients was higher [23].

In our study the 5 years survival rate in patients treated with chemotherapy was 56.1% and this study shows the effect of chemotherapy in increasing patients' survival. This effect similar to other studies [26,27].

Results of this study revealed that the mortality rate was 24%. Al-Shehab et al reported a mortality rate among children with ALL to be 25.4% which is slighltly higher than mortality rate found in this study [1]. However, this rate is higher than that reported by Alhadi et al , where the death rate was 6.2% [10].

Infection was the most cause of death 51.2 % , followed by combination of bleeding and infection 31.7% , then bleeding only 12.2 % , this results were lower in the study done by Al-Shehab et al ,the infection were 37.8% and the bleeding were 11.1%. [1]

It should be noted that the present study has several limitations, including its retrospective design . Moreover, the study did not investigate the potential impact of other comorbidities or treatment modalities on the outcome of acute leukemia. Therefore, further studies with larger sample sizes and prospective designs are warranted to confirm these findings and explore potential risk factors for adverse outcomes in children with acute leukemia.

Chapter 5: Conclusion and Recommendations

The findings of this study conclude that:

About half of cases of acute lymphoblastic leukemia were in the age group from 1 to 5 years. Most of children with acute lymphoblastic leukemia develop complete bone marrow remission at day of 22 (about 83.6 %).

There is two third of known cases of acute lymphoblastic leukemia survive more than 5 years from date of diagnosis and about one fourth of all cases relapsed. About half cases of acute lymphoblastic leukemia in pediatric patients were cured, while less than fourth of all cases died and more than half of dead cases died due to infection.

Based on the findings of the study, the following recommendations would be considered:

The outcomes of acute lymphoblastic leukemia continue to improve with more long-term survivors, decrease complications and treatment side effects should become a major focus.

More efforts to maintain the patient's access to health care service and improving the delivery of care is essential to prevent the development of complications, leading to better outcome.

Efforts to maintain the patient's access to the treatment at pediatric leukemia center improving outcome of leukemia.

Modification of health care services for children with leukemia to become more patient-centered, flexible and comprehensive may reduce time spent at pediatric leukemia center and also improve treatment outcomes.

Future research could focus on identifying factors affecting the outcome and causes of death among children with leukemia.

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References

1. Al-Shehab MA, Alhadi AM, Elnemr MAM, Al-Qadasi FA, Alabsi NA, et al. Epidemiological, Clinical and Paraclinical Characteristics of Childhood Acute Lymphoblastic Leukaemia in Sana'a, Yemen. Journal of Clinical & Diagnostic Research. 2020. 14.
2. Kipps TJ, Stevenson FK, Wu CJ, Croce CM, Packham G, et al. Chronic lymphocytic leukaemia. Nat Rev Dis Primers. 2017. 3: 16096.
3. Al-Ghazaly J, Al-Dubai W, Abdullah M. Pattern of adult leukemia at Al-Jomhori educational hospital, Sanaa, Yemen. Yemeni journal for medical sciences. 2014. 8.
4. American Cancer Society. 6e Global Economic Cost of Cancer, American Cancer Society, Atlanta, GA, USA, 2010.
5. Al-Maktari LA, Al-Nuzaili MA, Al-Shamahy HA, Al-Hadi AA, Ishak AA, et al. Distribution of hematological parameters counts for children with leukemia in children's cancer units at Al-Kuwait Hospital, Sana'a City: A Cross-Sectional Study. Adv Can Res Clinical Imag. 2021. 3: 2021.
6. Seth R, Singh A. Leukemias in children. The Indian Journal of Pediatrics. 2015. 82: 817-824.
7. Leukaemia Statistics, Australia Cancer Society, 2017. https:// leukaemia.canceraustralia.gov.au/statistics.
8. Seiter K. Acute myeloid leukemia staging: WebMD LLC. 2018. https://emedicine.medscape.com/article/2006750-overview.
9. Terwilliger T, Abdul-Hay M. Acute lymphoblastic leukemia: a comprehensive review and 2017 update. Blood cancer journal. 2017. 7: e577.
10. Alhadi A, El-Zine M, IshaK A, Al-Shamahy H. Childhood leukemia in yemen: the main types of childhood leukemia, its signs and clinical outcomes. EC Paediatrics. 2021. 10: 75-82.
11. Badheeb A, Baamer A. The pattern and distribution of malignancies reported in Hadhramout Sector, Yemen-2002-2011. Alandalus For Soc Appl Sci J. 2012.5: 7-16.
12. Satyanarayana L, Asthana S, Preeti Labani S. Childhood cancer incidence in India: A review of population-based cancer registries. Indian pediatrics. 2014. 51: 218-220.
13. Miller TP, Li Y, Kavcic M, Troxel AB, Huang YS, et al. Accuracy of Adverse Event Ascertainment in Clinical Trials for Pediatric Acute Myeloid Leukemia. J Clin Oncol. 2016. 34: 1537-1543.
14. WHO. Cancer children in Yemen face the - WHO EMRO.
15. Bawazir AA. Cancer incidence in Yemen from 1997 to 2011: a report from the Aden cancer registry. BMC Cancer. 2018. 18: 540.
16. Pui CH, Schrappe M, Ribeiro RC, Niemeyer CM. Childhood and adolescent lymphoid and myeloid leukemia. Hematology Am Soc Hematol Educ Program. 2004. 118-45.
17. Zou Y, Wang H, Chen XJ, Wang SC, Zhang L, et al. Study of clinical outcome and analysis of prognosis related factor in children with acute myeloid leukemia. Zhonghua Xue Ye Xue Za Zhi. 2006. 27: 621-625.
18. Powell JE, Mendez E, Parkes SE, Mann JR. Factors affecting survival in White and Asian children with acute lymphoblastic leukaemia. Br J Cancer. 2000. 82: 1568-1570.
19. Wessels G, Hesseling PB, Buurman M, Oud C, Nel ED. An analysis of prognostic variables in acute lymphocytic leukaemia in a heterogenous South African population. J Trop Pediatr. 1997. 43: 156-161.
20. Chessells JM, Hardisty RM, Richards S. Long survival in childhood lymphoblastic leukaemia. Br J Cancer. 1987. 55: 315-319.
21. Gaynon PS, Trigg ME, Heerema NA, Sensel MG, Sather HN, et al. Children's Cancer Group trials in childhood acute lymphoblastic leukemia: 1983-1995. Leukemia. 2000. 14: 2223-2233.
22. Schrappe M, Reiter A, Zimmermann M, Harbott J, Ludwig WD, et al. Longterm results of four consecutive trials in childhood ALL performed by the ALL-BFM study group from 1981 to 1995. BerlinFrankfurt-Munster. Leukemia. 2000. 14: 2205-2222.
23. Zareifar S, Almasi-Hashiani A, Karimi M, Tabatabaee SH, Ghiasvand R. Five-year survival rate of pediatric leukemia and its determinants. Koomesh. 2012. 14: 13-19.
24. Hazar V, Karasu GT, Uygun V, Akcan M, Kupesiz A, et al. Childhood acute lymphoblastic leukemia in Turkey: factors influencing treatment and outcome: a single center experience. J Pediatr Hematol Oncol 2010. 32: 317-322.
25. Moricke A, Reiter A, Zimmermann M, Gadner H, Stanulla M, et al. Risk-adjusted therapy of acute lymphoblastic leukemia can decrease treatment burden and improve survival: treatment results of 2169 unselected pediatric and adolescent patients enrolled in the trial ALL-BFM 95. Blood. 2008. 111: 4477-4489.
26. Liang DC, Chan TT, Lin KH, Lin DT, Lu MY, et al. Improved treatment results for childhood acute myeloid leukemia in Taiwan. Leukemia. 2006. 20: 136-141.
27. Buckley JD, Lampkin BC, Nesbit ME, Bernstein ID, Feig SA, et al. Remission induction in children with acute non-lymphocytic leukemia using cytosine arabinoside and doxorubicin or daunorubicin: a report from the Childrens Cancer Study Group. Med Pediatr Oncol. 1989. 17: 382-390.