Republic of Yemen
Ministry of Higher Education and Scientific Research
21 SEPTEMBER UNIVERSITY
FACULTY OF MEDICINE

الجمهورية اليمنية
وزارة التعليم العالي والبحث العلمي
جامعة ٢١ سبتمبر للعلوم الطبية والتطبيقية
كلية الطب البشري
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Relapse among Children with Acute Lymphoblastic Leukemia in Leukemia Center at Al-Kuwait Hospital, Sana'a City, during 2020 - 2021

By group D5a

Abd Alsamad Rageh Al-Awlaqi
Afkar Kamel Al-Sharabi
Ahmed Ali Al-Obari
Akram Fua'ad Al-Sofi
Amal Yahia Al-Dhabi
Amany Abdalaziz Al-Muhaya
Amera Mohammed Solh
Arif Abdallah Shamlan
Asma'a Nageeb Iskander
Bassam Ali Al-Yemeni
Husam Talal Al-samet
Ibrahim Salah Abo Horia

Under Supervision of

Dr. Amal Al-Morissi
Pediatrician doctor in Al-Kuwait hospital

Dr. Basheer Al-Nabehi
Assistant Pro. Of Community Medicine

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الانتكاسة عند الأطفال المصابين بإبيضاض الدم الليمفاوي الحاد في مركز سرطان الدم بمستشفى الكويت خلال ٢٠٢٠-٢٠٢١م

الباحثون

إبراهيم صالح أبو حورية
أحمد علي العبري
أسماء نجيب اسكندر
أفكار كامل الشرعبي
أكرم فؤاد الصوفي
آمال يحيى الظبي
أماني عبدالعزيز المحيا
أميرة محمد صلح
بسام علي اليمني
حسام طلال الصامت
عارف عبدالله شملان
عبدالصمد راجح العولقي

المشرفون

د/ امل المريسي
أخصائية أطفال
د. بشير النابهي
أستاذ مساعد طب مجتمع.

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Dedication

To those who illuminate spiritually our dreams; to those who sacrifice their rights to satisfy us for sharing our goals and targets.

To our blessed families whose love is thrilled to the core and full of passion. To our parents who did the best to make us great . To those who gift us the compassion of science an knowledge. To our doctors and teachers who were honest accompany .

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Abstract

Background : Acute lymphoblastic leukemia is a cancer of lymphoid line of blood cells which is characterized by developmental of large number of immature lymphocytes. Leukemia is the commonest cancer among Yemeni children an adult . Most cases with leukemia are treated by chemotherapy , during these cases relapse can occur and the central nervous system is a common site for relapse in acute lymphoblastic leukemia . Our research based study design to check relapse among patients with acute lymphoblastic leukemia .

Objective : the present study aims to determine the relapse that occurs among patients with acute lymphoblastic leukemia in pediatric leukemia center in Al-Kuwait hospital Sana'a City , from 1 January 2020 to 31 December 2021 .

Methodology : A descriptive retrospective study was conducted on children with leukemia who were treated in pediatric leukemia unit at Al-Kuwait University Hospital in Sana'a city .The sample size included 106 children diagnosed with cancer in pediatric leukemia center in Al-Kuwait hospital Sana'a City , from 1 January 2020 to 31 December 2021, data was collected from files, and analyzed by using SPSS (Statistical Package for Social sciences) .

Result : Out of 106 of cases of children with acute lymphoblastic leukemia who had a relapse in general were only 12 cases, with a rate of (11.3%) of the research sample , eight of them had CNS relapse , three had hematological and only one case had testicular relapse .

In CNS relapse: five cases within the age group (1-5) years; With a rate of (62.5) , One case in the age group (6-10) years , With a rate of (12.5%) , two cases within the age group (11-16) years With a rate of (25%) .

In hematological relapse : .two cases within the age group (1-5) years; with rate of 66.7%) of the cases affected by hematological relapse ,with rate of (4.5%) ,Only one case had a hematological relapse within the age group(6-10) years , with rate of (33.3%) , There is no cases of hematological relapse within the age group (11-16) years.

In testicular relapse , only one case of had this type of relapse , with a rate of (100%) , within the age group (6-10) years,

Conclusions:

106 Cases had acute lymphoblastic leukemia, the most of them had B cells type of leukemia ,including (63.2%) were males, and (36.8%) were females. Most of these cases on regular treatment with rate of 89%, and 55% of cases were at high risk.

(11.3%) of Cases had a relapse, which including (7.5%) of cases with CNS relapse, (2.8%) of cases with hematological relapse, and only (0.9%) of cases with testicular relapse. Most of relapses were at (1-5) years of age, and with regard to sex, they were equal between males and females . Also most of relapses were at high risk.

Key words: leukemic , Relapse, Acute lymphoblastic leukemia, ALL .

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Abbreviations

- **ALL:** Acute Lymphoblastic Leukemia**.**
- **AML:** Acute Myelogenous Leukemia**.**
- **BM:** Bone Marrow**.**
- **CML:** Chronic Myelogenous Leukemia**.**
- **CNS:** Central Nervous System **.**
- **FAB :** French ,American and British classification .
- **HLA:** Human Leukocyte Antigen .
- **HRs:** Hazard Ratios**.**
- **OS:** Overall Survival.
- **SPSS : S**tatistical Package of Social Sciences
- **WBC:** White Blood Cells.

Chapter one
Introduction

1.1 Background:

Blood and bone marrow constitute one of the largest organs in the body and it is an important potential target organ of chemical exposure. **(Lund JE. Feldman BF,2000)**

The bone marrow is found within the central cavities of axial and long bones. It consists of hematopoietic tissue islands and adipose cells surrounded by vascular sinuses interspersed within a meshwork of trabecular bone. It accounts for approximately 3% of the body weight in adult rats**. (Schermer S, 1967)**

The bone marrow is the major hematopoietic organ, and a primary lymphoid tissue, responsible for the production of erythrocytes, granulocytes, monocytes, lymphocytes and platelet. **(Jain NC,1986)**

The Hematopoiesis is the process by which multipotent hematopoietic stem cells differentiate into either myeloid or lymphoid precursor cells and, eventually, into mature blood cells. **(Gartner LP, 2017)**

The Myeloid precursor cells develop into erythrocytes, granulocytes, or megakaryocytes. Whereas Lymphoid precursor cells develop into lymphocytes or natural killer cells, **(MurkeF,2017)**

The Lymphocyte has two main types ; T cells (which mediate cellular immunity) and B cells (which mediate humeral (immunity), **(Davidson)**

Haematological malignancies arise when the processes proliferation or apoptosis are corrupted in blood cells because of controlling acquired mutations in key regulatory genes . Thus a condition called Leukemia which is malignant disorders of the hematopoietic stem cell compartment ,characteristically associated with increased numbers of white cells in the bone marrow and/ or

peripheral blood. If more primitive stem or progenitor cells are involved, the cells can have the highest growth fractions of all human progressive, life-threatening illnesses such as the neoplasms, producing rapidly acute leukemia. **(Davidson.)**

Acute lymphoblastic leukemia (ALL) is a cancer of the lymphoid line of blood cells characterized by the development of large numbers of immature lymphocytes. Symptoms may include feeling tired, pale skin color, fever, easy bleeding or bruising, enlarged lymph nodes, or bone pain **. (National Cancer Institute, 2017)**

As an acute leukemia is progresses rapidly and typically fatal within weeks or months if left untreated. **(Inaba H, Greaves M, Mullighan CG 2013)**

The excessive immature lymphocytes in the bone marrow interfere with the production of new red blood cells, white blood cells, and platelets (Davidson.)Diagnosis is typically based on blood tests and bone marrow examination **(Ferri, Fred F, 2017**)

Acute lymphoblastic leukemia is typically treated initially with chemotherapy aimed at bringing about remission. This is then followed by further chemotherapy typically over a number of years . **(Hunger SP, 2015)**

Treatment usually also includes intrathecal chemotherapy since systemic chemotherapy can have limited penetration into the central nervous system and the central nervous system is a common site for relapse of acute lymphoblastic leukemia. **(Inaba H, June 2013 ,Vora, 2017)**

Treatment can also includes radiation therapy if spread to the brain has occurred . Stem cell transplantation may be used if the disease recurs following standard treatment. Additional treatments such as chimeric antigen receptor T cell immunotherapy are being used and further studied. **(Hunger SP, 2015)** .

Typically, people who experience a relapse in their ALL after initial treatment have a poorer prognosis than those who remain in complete remission after induction therapy. It is unlikely that recurrent leukemia will respond favorably to the standard chemotherapy regimen that was initially implemented, and instead, these people should be trialed on reinduction chemotherapy followed by allogeneic bone marrow transplantation. These people who have relapse may also receive blinatumomab, as it has shown to increase remission rates and overall survival rates, without increased toxic effects **(National Cancer Institute, 2017)**

Low dose palliative radiation may also help reduce the burden of tumor inside or outside the central nervous system and alleviate some symptoms. Recently, there has also been evidence and approval of use for dasatinib, a tyrosine kinase inhibitor. It has shown efficacy in cases of people with Ph1-positive and imatinib-resistant ALL, but more research needs to be done in the long-term survival and time of relapse. **(Kantarjian H, Stein A, Gökbuget N, , et al., 2017)**

1.2 Epidemiology :

Acute lymphoblastic leukemia (ALL)is classified according to cell lineage as either B-lineage or T-lineage. The incidence of ALL peaks at 2 to 5 years of age and is higher in boys than in girls. T-cell ALL, in particular, is associated with male predominance as well as an older age of peak **(Nelson, n.d.)**

Globally ,the highest incidence of ALL occurs in Italy, the United States, Switzerland, and Costa Rica In Europe overall, B-cell precursor ALL has been increasing by around 1% each year. **(Nelson R. 2018)**

ALL is the most common type of cancer and leukemia in children in the United States. Median age at diagnosis is 17 years **(National Institutes of Health., 2021)** Acute lymphoblastic leukemia accounts for 74% of pediatric leukemia cases **(Cancer Fact ,Figure , 2021)**

In adults, ALL is less common than acute myeloid leukemia (AML) (**Cancer Fact ,Figure , 2021)**

Each year 2500 to 3500 new cases of childhood leukemia occur in the United States. The disease affects about 40 per 1 million children under the age of 15 years. ALL accounts for approximately 75% of cases. Acute myelogenous leukemia (AML) accounts for 15% to 20%, and CML accounts for less than 5% of cases. Other chronic leukemia, including juvenile myelomonocytic leukemia, chronic myelomonocytic leukemia, and chronic lymphocytic leukemia, are rare in childhood incidence. In the United States ALL is more common in white than in African American children **(Essential Nelson)**

Acute lymphoblastic leukemia is diagnosed in approximately 3,100 children and adolescents <20 yr. old in the United States each year. ALL has a striking peak incidence at 2-3 yr. of age and occurs more in boys than in girls at all ages.

This peak age incidence was apparent decades ago in white people on advanced socioeconomic countries, but it has since been confirmed in the black population of the United States as well. The disease is more common in children with certain chromosomal abnormalities, such as Down syndrome, Bloom syndrome, ataxia-telangiectasia, and Fanconi anemia. Among identical twins, the risk to the second twin if one twin develops leukemia is greater than that in the general population. The risk is >70% if ALL is diagnosed in the first twin during the 1st yr of life and the twins shared the same (monochorionic) placenta. If the first twin develops ALL by 5-7 yr. of age, the risk to

the second twin is at least twice of the general population, regardless of zygosity **(Essential Nelson)**

Most common cancer among Yemeni children and adults were leukemia (33.1%). **(Bawazir AA, 2018**)

Between 10% and 20% of patients, who have achieved complete remission after initial treatment for ALL, will have a relapse.

In children, the relapse rate is near to 10%, while in adults relapse rate is closer to 50%. Relapse of ALL generally occurs within two years of initial treatment, although it may occur several months to years after the initial remission .

1.3 Etiology :

In most cases, the cause is unknown **(Hunger SP, 2015)** . Genetic risk factors may include Down syndrome, Li–Fraumeni syndrome, or neurofibromatosis type 1 **(National Institutes of Health**, **2017)** Environmental risk factors may include significant radiation exposure or prior chemotherapy .Evidence regarding electromagnetic fields or pesticides are unclear.(**Inaba H, 2013 ,Vora, 2017**).

Regarding immunology and epidemiology of childhood leukemia ,Greaves concluded that B-cell precursor acute lymphoblastic leukemia (ALL) has a multifactorial etiology, with a two-step process of genetic mutation and exposure to infection play a prominent role. The first step occurs in utero, when fusion gene formation or hyperdiploidy generates a covert, pre-leukemic clone. The second step is the postnatal acquisition of secondary genetic changes that drive conversion to overt leukemia. Only 1% of children born with a pre-leukemic clone progress to leukemia. (**Greaves M.A, 2018**)

The second step is triggered by infection. Triggering is more likely to occur in children whose immune response is abnormally regulated because they were not exposed to infections in the first few weeks and months of life. Lack of exposure to these early infections, which prime the immune system, is more likely to occur in societies that are zealous about hygiene; this would help explain why at present, pediatric ALL is seen primarily in industrialized societies. (**Greaves M.A, 2018**)

Chapter two
Literature review

In many researches there are different results about this study but in Yemen there is only one study : 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 , 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) , 244 leukemia patients were diagnosed, treated and followed up with mean ±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%) , 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 (Al-Shamahy , 2021).

Other study is in Relapsed childhood acute lymphoblastic leukemia in Upper Egypt :

relapse is the main reason of treatment failure in childhood acute Lymphoblastic leukemia (ALL), Aim: To study the treatment outcome of first ALL relapse in response to two different reinduction regimens and prognostic factors predicting outcome , a retrospective study that included 82 children with ALL in the 1st relapse from two tertiary oncology centers in Upper Egypt. Patients were treated according to the St. Jude ALL-R16 protocol. Seventeen patients were treated with a standard reinduction (regimen 1) and 65 were treated with a modified reinduction regimen in which anthracycline was added and asparaginase was reduced to 9 doses (regimen 2). Response, survival and prognostic factors were analyzed. Second, complete remission (CR2) was achieved in 57% of all patients (65% with regimen 2 vs. 29% with regimen 1, p = 0.009). FLAG regimen resulted in achieving CR2 in all patients with reinduction failure , treatment mortality was more common with regimen 2 than with regimen 1 (34% vs. 12%, respectively). For all patients, the 2-year overall and event-free survival rates were 30% and 25%. In multivariate analysis, high initial total leukocytic count, isolated medullary relapse, regimen 1 and very early relapse were independently associated with worse event free survival (p = 0.031, 0.017, 0.037 and 0.001; respectively) , the overall outcome of treatment of first ALL relapse in children in our region is poor. New intensive chemotherapy regimens may help in improving the treatment outcome. Acute Lymphoblastic Leukemia, First relapse, Children, Survival, Prognostic factors, Egypt . (Azza Shibl, 2021) Other examples are in Relapsed childhood acute lymphoblastic leukemia in the Nordic countries: prognostic factors, treatment and outcome: relapse is the main reason for treatment failure in childhood acute lymphoblastic leukemia. Despite improvements in the up-front therapy, survival after relapse is still relatively poor, especially for high-risk relapses. The aims of this study were to assess outcomes following acute lymphoblastic leukemia relapse after common initial Nordic Society of Pediatric Haematology and Oncology protocol treatment; to validate currently used risk stratifications, and identify additional prognostic factors for overall survival. Altogether, 516 of 2735 patients (18.9%) relapsed between 1992 and 2011 and were included in the study. There were no statistically significant differences in outcome between the up-front protocols or between the relapse protocols used, but an improvement over time was observed. The 5-year overall survival for patients relapsing in the period 2002–2011 was 57.5±3.4%, but 44.7±3.2%)p <0.001) if relapse occurred in the period 1992–2001.

Factors independently predicting mortality after relapse included short duration of first remission, bone marrow involvement, age ten years or over, unfavorable cytogenetic, and Down syndrome. T-cell immunophenotype was not an independent prognostic factor unless in combination with hyperleukocytosis at diagnosis, the outcome for early combined pre-B relapses was unexpectedly poor (5-year overall survival 38.0±10.6%), which supports the notion that these patients need further risk adjustment. Although survival outcomes have improved over time, the development of novel approaches is urgently needed to increase survival in relapsed childhood acute lymphoblastic leukemia.

Another study Relapse of childhood acute lymphoblastic leukemia and outcomes at a reference center in Latin America: organomegaly at diagnosis is a significant clinical predictor in 2018 Jan. Relapse is the major cause of treatment failure in acute lymphoblastic leukemia (ALL) of childhood; it is more frequent among high-risk patients from low-middle income than from high-income countries. The frequency, sites and outcome of relapsed ALL in children of northeast Mexico over a decade was documented, a retrospective analysis of 246 children belonging to a low-income group <16 years with de novo ALL during 2004-2015 was performed, Five-year overall survival (OS) and event-free survival was estimated by Kaplan-Meier analysis. Data on time, site, response to therapy and final outcome of relapse were analyzed. Hazard ratios (HRs) of relapse and death were estimated by the Cox regression model. Very early relapse was defined as that occurring in <18 months, early relapse between 18 and 36 months, and late relapse >36 months from diagnosis, respectively , eighty-seven (35.4%) children relapsed. Five-year OS was 82.6% in children without relapse vs. 42% for relapsed patients. Bone marrow (BM) was the most frequent site of relapse (51.72%). Isolated central nervous system (CNS) relapses occurred in 29.9%. Five-year OS was 11.2% for BM and 15.5% for early relapse. HR of relapse for organomegaly was 3.683, 2.247 for an initial white blood cell count >50 000 × 109/l and 1.169 for positive minimal residual disease status , a high rate of very early, CNS, and BM relapse with a considerably low 5-year OS requiring reassessment of therapy was documented. Organomegaly at diagnosis was a highly significant clinical predictor for relapse , acute lymphoblastic leukemia; Latin America; low-middle-income country; pediatric hematology; relapse; survival rates. (José Carlos Jaime-Pérez et al ,2018) .

Another study :

Relapsed Childhood Acute Lymphoblastic Leukemia: Experience from a Single Tertiary Center in Thailand 2021 ,the outcomes of relapsed childhood acute lymphoblastic leukemia (ALL) in developed countries have improved over time as a result of risk-adapted, minimal residual disease-directed therapy, hematopoietic stem cell transplantation, and immunotherapy. There are few studies that have examined survival in relapsed childhood ALL in resource-limited countries. Therefore, this study aimed to assess the prognostic factors and survival outcome of relapsed childhood ALL in a major tertiary center in Southern Thailand , the medical records of patients with ALL aged <15 years between January 2000 and December 2019 were retrospectively reviewed. The Kaplan-Meier method was used to depict the overall survival (OS) , a total of 472 patients with ALL were enrolled and relapsed ALL was found in 155 (32.8%) patients. Of these, 131 (84.5%) and 24 (15.5%) had B-cell and T-cell phenotypes, respectively. One hundred thirteen (72.9%) and 42 (27.1%) patients had early and late relapses, respectively. The most common site of relapse was bone marrow in 102 patients (65.8%). One hundred twenty-eight (82.6%) patients received treatment while 27 (17.4%) patients refused treatment. The 5-year OS of all relapsed patients was 11.9%. The 5-year OS among the patients with early relapse was significantly lower than in the patients with late relapse (5.3% vs. 29.1%, respectively, p <0.0001). Site and immunophenotype were not associated with survival of relapsed ALL. The median survival times among the patients who received and refused relapse chemotherapy were 11.8 and 3.1 months, respectively (p <0.0001) , the relapse rate accounted for one third of patients with ALL with the 5-year OS of 12%. Early relapse and those who refused treatment were associated with poor survival outcome , relapsed childhood acute lymphoblastic leukemia; resource-limited countries; survival outcome (Thirachit Chotsampancharoen et al,) .

Another study: Retrospective Study on Very Early Relapse of Childhood Acute Lymphoblastic Leukemia at a Reference Centre in Indonesia , the cure rate of Acute Lymphoblastic Leukemia (ALL) in low and middle-income countries is still low. Many factors contribute to relapses event, thus leading to failure of the treatment outcome. However, there are limited studies regarding the relapse of childhood cancer in

Indonesia. This study determined demography, clinical, and characteristic laboratory differentiation between relapse and non-relapse in the bone marrow childhood ALL group , this was a retrospective descriptive study in children newly diagnosed with ALL ages 0-18 who completed the induction phase using the 2013 treatment protocol during the 2018 period in Pediatrics Hematology-Oncology Unit at a reference center hospital in Indonesia. Of 78 data collected from the Indonesian Pediatric Cancer Registry (IP-CAR) and Hospital Information System after excluding abandoned treatment or death during treatment, only 35 patients completed the overall therapy. We evaluated bone marrow relapse and classified it into 'very early' relapse that occurs at least 18 months from diagnosis, 'early' relapse between 18 and 36 months, and more than 36 months is called 'late' relapse. Chi-square test was used to elaborate association between relapse and sex, leukocyte count, morphological classification, risk stratification, nutritional status. Kruskal Wallis tests were used to elaborate on the association between relapse, age, and induction duration. P value<0.05 was considered statistically significant , among 35 patients in this study, seven patients experienced bone marrow relapse. Relapses were dominant in four male patients, four patients aged from 1-10 years old, six patients with leukocytes count below 50.000/mm3, six normal nutritional status patients, and six patients classified as L2 patients. All relapse events occurred in a very early stage. Four patients are classified as standard risk, and three patients are high risk. There were no significant differences among characteristics of the relapse and non-relapse groups ,the observed relapse onset is less than 18 months from diagnosis (very early relapse) during maintenance treatment. However, we found no significant demography, clinical, and laboratory differentiation between relapse and non-relapse groups , acute lymphoblastic leukemia childhood leukemia clinical demography laboratory characteristic low-middle income country very early relapse (Swedish Childhood Cancer Foundation,2015).

Chapter three
Objectives

3.1 Aim of study:

• To determine the relapse occur among patients with acute lymphoblastic leukemia in Pediatric Leukemia Center in Al-Kuwait Hospital , Sana'a City, during (2020 – 2021) according to local statistics.

3.2 Specific objectives:

• To assess the kind of relapse with acute lymphocytic leukemia in the pediatrics age group.
• To determine the relapses' case according to gender and age more common occur.
• To determine with relapses' cases, which type of risk .
• To determine at which stage of treatment relapse occurs .
•To determine in relapse cases , the number of WBC count at time of diagnosis .

3.3 Hypothesis of the study:

•There are statistically significant differences at the level of significance (≤0.05) due to the variables (sex).
•There are statistically significant differences between the types of relapse and WBC coun.

Chapter four
Material & Methodology

4.1 Study design :

A retrospective cross sectional descriptive observational study of childhood interval during2020- 2021. The study is 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 is based on clinical examination by a specialist (signs and symptoms that indicate the child may have leukemia such as swollen lymph nodes, areas of bleeding, bruising ,fever ,bone pain ,dizziness, fatigue , dyspnea , sweating , loss of weight , recurrent infection and pallor) which confirmed by blood film examination , histological bone marrow study and HLA (Human Leukocyte Antigen) .

4.2 Study site :

The present study was in leukemic center in Alkuwait hospital in Sana'a city, Yemen.

4.3 Study duration :

The study lasted for five months (from August to December 2022).

4.4 Sample size :

study sample included 106 children selected randomly& diagnosed with cancer in Alkuwait hospital during 2020- 2021.

4.5 Data collection :

data collection is depends on retrospective 106 files at the leukemic center in Alkuwait hospital during 2020 – 2021. Those files must have full information.

The data including qualitative (name , gender, types of leukemia, , clinical signs, outcomes) and quantitative (age ,WBC count). Group diagnoses and histopathological diagnoses were made according to French, American and British classifications (FAB) of childhood leukemia .

4.6 Data analysis :

Collected data were analyzed by using SPPS (statistical package for social since) program for static analysis, version 22 (IBM, Armonk, NY).

Statistical analysis included quantitative descriptive analysis and summary of statistics describe the frequency of diagnostic groups and subgroups of childhood cancer, in addition to survival data using at the Kaplan-Meier survival curve.

4.7 Sampling technique :

A106 files are selected randomly from leukemic center in Alkuwait hospital. Data were collected by research form from files. The total study population n= 283 patients.

4.8 Inclusion and Exclusion criteria :

- **The Inclusion criteria were included:**

1- A child at any age who was diagnosed and still treated in AL-Kuwait hospital during (2020-2021) .
2- A child who has full information according to research form .

- **The exclusion criteria include :**

1- A child who was diagnosed and treated before 2020 .
2- A child with other type of leukemia such as AML
3- A child who doesn't have flowcytometry .
4- A child who has incomplete files .

4.9 Ethical Considerations :

The study protocol was passed by Ethical committee of 21 September University in the Educational Republican Hospital by it's protocols was obtained prior to carrying out this study ,all obtained data will be confidential and will not be used for Purposes other than scientific research.

Chapter five
Result

1. Demographic data :

Total of 106 of acute lymphoblastic leukemia patients were the main age ±SD (6.08±0.793) , the average age was (1- 16 years) ,where the male represent 67 (63.2%) , where female represent 39 (36.8%) and most of patients were B cell type were represent 80 (75.5 %) , were T-cell 26 (24.5%) . (Table 1) .

It is clear that the children with acute lymphoblastic leukemia in Al-Kuwait Hospital were mostly from Sana'a governorate with a rate of (19.8%), followed by children from Thamar governorate with a rate of (13.2%), and then children from the governorates of Hajah and Ibb, with a rate of (11.3%) for both ,these percentages are considered normal because most of the children in the research sample are from Sana'a and the nearby governorates, research was conducted in Sana'a, so children with acute lymphocytic leukemia in Kuwait Hospital in Sana'a, who came from remote governorates, had a lower percentage so, these characteristics are considered normal and reflect the size of the community, as it included children with acute lymphocytic leukemia from most Yemeni governorates, and this feature enhances the results of field research and can be trusted. (Table 2)

The vast majority of children with acute lymphocytic leukemia were response to treatment after induction, with a rate of (97.2%).(Table3)

The demographic data of (age , sex , flow cytometry , WBC count and regularity of treatment, the majority of children in rate of (88.7%) with acute lymphocytic leukemia were on regular treatment , and that (11.3) on irregular treatment. (Table 4)

On other hand, the characteristic of type of risk in acute lymphoblastic patients showed that the children who were at high risk due to acute lymphoblastic leukemia were (54.7%), and the percentage of children at lower risk due to the same disease was (45.3%). (Table 5)

2. Statistical data :

The characteristic of data according to type of relapse among acute lymphoblastic patients through that the total cases of children with acute lymphoblastic leukemia who had a relapse in general were only 12 cases, with a rate of (11.3%) of the research sample consisting of 106 cases and there is no statistical correlation significantly p value (0.482) (Table 6)

We note that most of the relapses that occurred among the children with acute lymphocytic leukemia were within the age group (1-5) years, with a total of (7) cases, at a rate of (58.3%) of the total of cases of children with acute lymphocytic leukemia that occurred relapse was with a rate of (15.9%) of the total of cases of children with acute lymphoblastic leukemia who had a relapse within this age group (1-5) years, and with a rate of (6.6%) of the total research sample. As for the

cases of children within the age groups (6-10) years who had a relapse, there were only 3 cases, with a rate of (25.0%), of the total of cases of children with acute lymphoblastic leukemia who had relapse and with a rate of (7.1%) of the total of cases of children with acute lymphoblastic leukemia who had a relapse within this age group (6-10) years, and the rate is (2.8%) of the total research sample. Regarding cases of children within the age groups (11-16) years who had a relapse, there were 2 cases, with a rate of (16.7%), of the total of cases of children with acute lymphoblastic leukemia who had relapse; (12 cases), and with a rate of (10.0%) of the total of cases of children with acute lymphoblastic leukemia who had a relapse within the age group (11-16) years, and the rate is (1.9%) of the total of the research sample. Five cases within the age group (1-5) years; With a rate of (62.5%) of cases effected with this type, and this is the same percentage of cases with CNS relapse of effected cases that had a relapse of any of the three types of relapse within the age group (1-5) years. One case in the age group (6-10) years; with (12.5%) of the cases effected with this type and by (2.4%) of the effected cases who had a relapse of any of the three types of relapse within the age group (6-10) years.

Only two cases within the age group (11-16) years; (25%) of cases with CNS relapse , and (10.0%) of cases with relapse of any of the three types of relapse within the age group (11-16) years.As for the cases with acute lymphocytic leukemia that had hematological relapse , there were three cases, with a rate of (2.8%) of the cases of children with acute lymphocytic leukemia that had a relapse of this type according to the age group .

Two cases within the age group (1-5) years; with (66.7%) of the cases affected by hematological relapse ,and with (4.5%) of the affected cases who had a relapse with any one of the three types of relapse within the age group (1-5) years. Also Only one case had a hematological relapse within the age group(6-10) years; with (33.3%) of the cases affected with this type, and with (2.4%) of the affected cases who had a relapse of any type of the three types of relapse within the age group(6-10) years. And there are no cases of hematological relapse within the age group (11-16) years. The results also show that there was only one case of children with acute lymphocytic leukemia who had a testicular relapse , with a rate of (100%) of the cases of children with acute lymphocytic leukemia within this type of relapse, and it was within the age group (6-10) years, with a rate of (2.4%) of the total of cases of children with acute lymphocytic leukemia, which had a relapse from any of the three types of relapse. , there is no stastical correlation significantly p value (0.309) . Table (7)

we note that the relapses that occurred among children with acute lymphocytic leukemia tended to female children, with a total of (6) cases, with a rate of (50%) of the total cases of children with

acute lymphocytic leukemia who had a relapse; (12 cases), with a rate of (15.4%). Of the cases of female children in the sample, at a rate of (5.7%) of the total of research sample; (106 cases), as the data of the previous table shows that the relapses that occurred among male children with acute lymphocytic leukemia were in sex male cases, at a rate of (50%) of the total of cases of children with leukemia. Regarding patient with acute lymphoblastic leukemia relapse; (12 cases), with a rate of (9.0%) of the cases of male children in the sample, and with a rate of (5.7%) of the total research sample that had a relapse (regardless of the type of relapse).

To clarify more about the types of relapses that occurred among cases of children with acute lymphocytic leukemia, according to the type of relapse, and gender, we list the results as follows:

Type of relapse (CNS) by gender: There were three cases of males with CNS relapse with a rate of (37.5%) of the cases that had a relapse of this type , and with a rate of (4.5%) of the cases of male children, and with a rate of (2.8%) of the total of cases that had relapses in general (regardless of the type of relapse).

Five female cases with CNS relapse, with a rate of (62.5%) of the cases that had a relapse of this type , and with a rate of (12.8%) of the cases of female children in the females, and with a rate of (4.7%) of the total cases that had relapses in general (regardless of the type of relapse).

Hematological relapse by gender: Two male cases (66.7%) with hematological relapse , with a rate of (3.0) of male children, and with a rate of (1.9%) of the total cases that had relapses in general (regardless of the type of relapse). Only one female case had a hematological relapse, with a rate of (33.3%) of the cases affected with this type, with rate of (2.6) of female children and with a rate of (0.9%) of the total of cases that had relapses in general (regardless of the type of relapse) .

Testicular relapse by gender: Only 1 male case had a relapse of this type with (100%) of the cases with this type of relapse, with rate of (1.5) of male children and by (0.9%) of the total of cases that had relapses in general (regardless of the type of relapse) , there is stastical correlation significantly p value (0.04) . (Table8)

In the table (9) show that: In (CNS) relapse 5 of cases are at high risk with a rate of (62.5%) within type of relapse, with a rate of (8.6%) within type of risk, and with rate of (4.7%) of the total of cases that had relapse, also 3 cases had low risk with rate of (37.5%) within type of relapse, with a rate of (6.3%) within type of risk, and with rate of (2.8%) of total cases that had relapse. And only 3 cases of the hematological relapse had high risk with rate of (100%) within type of relapse, with

rate of (5.3%) within type of risk , and with rate of (2.8%) of total of cases that had a relapse and there are no cases have low risk. The testicular relapse had 1 case that is at high risk with rate of (100%) within type of relapse, with a rate of (1.7%) within type of risk, and with rate of (0.9%) of total of cases that had relapse, there is no stastical correlation significantly of high and low risk p value respectivlly (0.229 – 0.58).(Table 9)

Also, the cases that have a relapse with WBC count less than(5000) were 4 cases (33.3%) , cases that have a relapse with WBC count from (5000 to 10000) were 3 cases (25%) and cases that have a relapse with WBC count more than (10000) were 5 cases (41.7%) , there is stastical correlation significantly p value (0.007) . (Table10)

1-Demographic data :

Table (1) Characteristic of data according to age category ,sex and flow cytometry in acute lymphoblastic patients (2020/2021):

Age Category	Frequency	Percent
Mean ± SD	6.08±0.793	
01-05 Years	44	41.5%
06-10 Years	42	39.6%
11-16 Years	20	18.9%
Sex		
Male	67	63.2%
Female	39	36.8%
Flow cytometry		
B-cell	80	75.5%
T-cell	26	24.5%
Total	**106**	**100%**

Table (2) Characteristic of data according to the place (City in acute lymphoblastic patients (2020/2021):

City	Frequency	Percent
Sana'a	21	19.8%
Ibb	12	11.3%
Al baida`a	4	3.8%
Al hodaida	4	3.8%
Al mahweet	7	6.6%
Taiz	9	8.5%
Haja	12	11.3%
Hadramout	1	0.9%
Thamar	14	13.2%
Raima	5	4.7%
Shabua	1	0.9%
Sa`adah	6	5.7%
Amran	9	8.5%
Mareb	1	0.9%
Total	**106**	**100%**

Table (3) Characteristic of data according to time of response to treatment in acute lymphoblastic patients:

Time of response of treatment	Frequency	Percent
after induction	103	97.2%
no response after induction	3	2.8%
Total	**106**	**100%**

Table (4): Demographic data (Age, Sex) with laboratory test (Flow cytometry, WBC count) ,and regularity of treatment :

N	Age	Sex	Flow cytometry	WBC count /1000	Regular/irregular treatment
1	2	2	1	0.9	2
2	3	1	2	7.9	1
3	4	1	1	1.59	2
4	4	2	1	4.35	2
5	4	2	2	9.99	1
6	4	1	1	76	1
6					
7	5	2	1	32.1	1
8	7	2	2	1.51	2
9	7	1	2	16	1
10	9	2	1	44	1
11	12	2	1	8.3	1
12	12	1	1	40	2
Median	3.37	0.52	0.51	0.90	0.51
Range	(2-12)	(1-2)	(1-2)	(0.9-76)	(1-2)

Table (5) Frequency of regularity treatment and type of risk in acute lymphoblastic patients (2020/2021):

Regularity of Treatment	Frequency	Percent
Regular	94	88.7%
Irregular	12	11.3%
Type of Risk		
High Risk	58	54.7%
Low Risk	48	45.3%
Total	**106**	**100%**

2-Statistical Data:

Table (6): Characteristic of data according to type of relapse in acute lymphoblastic patients:

Type of Relapse	Mean ±SD	Frequency/%	Percent in relapse	Pearson Correlation	Significance P value
CNS		8 (7.5%)	66.7%		
Hematology		3 (2.8%)	25%		
Testicular		1(0.9%)	8.33%		
Total of Relapse	**1.4±.608**	**12(11.3%)**	**100%**	**1.000**	**0.482**
No Relapse	--	94 (88.7%)	88.7%		
Total	**--**	**106**	**---**		

Table (7) Characteristic of data per type of relapse per age category in acute lymphoblastic patients :

Type of Relapse / Age Category		Age Category (Years) (1-5)	(6-10)	(11-16)	Total	P value
CNS	**Count**	5	1	2	8	
	% within Type of relapse	62.5%	12.5%	25.0%	100.0%	
	% within age category	11.4%	2.4%	10.0%	7.5%	
	% of Total	4.7%	0.9%	1.9%	7.5%	
Hematology	**Count**	2	1	0	3	
	% within Type of relapse	66.7%	33.3%	0.0%	100.0%	
	% within age category	4.5%	2.4%	0.0%	2.8%	
	% of Total	1.9%	0.9%	0.0%	2.8%	0.309
Testicular	**Count**	0	1	0	1	
	% within Type of relapse	0.0%	100.0%	0.0%	100.0%	
	% within age category	0.0%	2.4%	0.0%	0.9%	
	% of Total	0.0%	0.9%	0.0%	0.9%	
Total (Type of Relapse)	**Count**	7	3	2	12	
	% within Type of relapse	58.3%	25.0%	16.7%	100.0%	
	% within age category	15.9%	7.1%	10.0%	11.3%	
	Percent of Total	6.6%	2.8%	1.9%	11.3%	0.309
Total of No Relapse	**Count**	37	39	18	94	
	% within Type of relapse	39.4%	41.5%	19.1%	100.0%	
	% within age category	84.1%	92.9%	90.0%	88.7%	
	Percent of Total	34.9%	36.8%	17.0%	88.7%	
Total of All	**Count**	44	42	20	106	
	% within Type of relapse	41.5%	39.6%	18.9%	100%	
	% within age category	100%	100%	100%	100%	
	Percent of Total	**41.5%**	**39.6%**	**18.9%**	**100%**	

Table (8) Characteristic of data according to type of relapse per sex in acute lymphoblastic patients :

Type of Relapse / Sex		Sex		Total	P value
		Male	Female		
CNS	**Count**	3	5	8	
	% within Type of relapse	37.5%	62.5%	100%	
	% within Sex	4.5%	12.8%	7.5%	
	% of Total	2.8%	4.7%	7.5%	
Hematology	**Count**	2	1	3	
	% within Type of relapse	66.7%	33.3%	100%	
	% within Sex	3.0%	2.6%	2.8%	
	% of Total	1.9%	0.9%	2.8%	
Testicular	**Count**	1	-	1	
	% within Type of relapse	100%	0%	100%	
	% within Sex	1.5%	0%	0.9%	
	% of Total	0.9%	0%	0.9%	
Total (Type of Relapse)	**Count**	6	6	12	
	% within Type of relapse	50%	50%	100%	0.04
	% within Sex	9.0%	15.4%	11.3%	
	Percent of Total	**5.7%**	**5.7%**	**11.3%**	

Table (9) Characteristic of data according to type of relapse per type of risk in acute lymphoblastic patients:

Type of Relapse / Type of Risk		Type of Risk		Total
		High Risk	Low Risk	
CNS	**Count**	5	3	8
	% within Type of relapse	62.5%	37.5%	100.0%
	% within Type of risk	8.6%	6.3%	7.5%
	% of Total	4.7%	2.8%	7.5%
Hematology	**Count**	3	0	3
	% within Type of relapse	100.0%	0.0%	100.0%
	% within Type of risk	5.2%	0.0%	2.8%
	% of Total	2.8%	0.0%	2.8%
Testicular	**Count**	1	0	1
	% within Type of relapse	100.0%	0.0%	100.0%
	% within Type of risk	1.7%	0.0%	0.9%
	% of Total	0.9%	0.0%	0.9%
P value		0.229	0.582	
Total (Type of Relapse)	**Count**	9	3	12
	% within Type of relapse	75.0%	25.0%	100.0%
	% within Type of risk	15.5%	6.3%	11.3%
	Percent of Total	8.5%	2.8%	11.3%

Table (10) Characteristic of data according to type of relapse per WBC count in acute lymphoblastic patients **:**

Type of Relapse / WBC		WBC Count			Total	P value
		Less than 5	5-10	More than 10		
CNS	**Count**	1	3	4	8	
	% within Type of relapse	12.5%	37.5%	50.0%	100.0%	
	% within results of WBC	2.3%	15.0%	9.5%	7.5%	
	% of Total	0.9%	2.8%	3.8%	7.5%	
Hematology	**Count**	3	0	0	3	
	% within Type of relapse	100.0%	0.0%	0.0%	100.0%	
	% within results of WBC	6.8%	0.0%	0.0%	2.8%	
	% of Total	2.8%	0.0%	0.0%	2.8%	
Testicular	**Count**	0	0	1	1	
	% within Type of relapse	0.0%	0.0%	100.0%	100.0%	
	% within results of WBC	0.0%	0.0%	2.4%	0.9%	
	% of Total	0.0%	0.0%	0.9%	0.9%	
Total (Type of Relapse)	**Count**	4	3	5	12	0.007
	% within Type of relapse	33.3%	25.0%	41.7%	100.0%	
	% within results of WBC	9.1%	15.0%	11.9%	11.3%	
	Percent of Total	3.8%	2.8%	4.7%	11.3%	

Chapter six
Discussion

Discussion:

The data were analyzed by using SPSS program, it was distributed according to age, gender, type of relapse, type of risk, WBC count, time of relapse according to treatment, and regularity of treatment Relapse of Acute Lymphoblastic Leukemia is catastrophic event that leads to greatly reduced chances of surviving, and it's the most common cause of treatment failure.

Relapse is occur among 12 (11.3%) of 106 children who were diagnosed and treated in Al- kuwait hospital during the study period (2020-2021), compared to another study in Yemen during the period (2014- 2018) when the relapse rate was (2%) **(Al-Shamahy, 2021)** , and in Egypt (2021), the relapse rate was (16.5**%)(Azza Shibl ,2021**), also in another study that was in Nordic countries the relapse rate was (35.4%) **(José Carlos Jaime-Pérez et al ,2018)** , while in Thailand, the relapse rate was (32.8%)**(Thirachit Chotsampancharoen et al, 2022)**.The commonest type of relapse in our study was CNS relapse, but study in egypt (2021) **(Azza Shibl , 2021)** . In Nordic countries, the hematological relapse were the common **(José Carlos Jaime-Pérez et al ,2018)**.

The study result show that the type of risk in relapsed patients were at high risk with rate of (75.0%) , while a study in Indonesia show that the relapsed patients had low risk more than high risk **(Swedish Childhood Cancer Foundation,2015).**

Regarding the gender, the prevalence of relapse was equal between males and females , but in another study in Yemen **(Al-Shamahy, 2021)** , and Egypt the males were more than females **(Azza Shibl , 2021)**.

The most affected children in our study with relapse were at age (1-5) years old with a rate (58.3%), while in another Yemeny study (2014-2018) was the age (11-15) years old**(Al-Shamahy, 2021)** , in Egypt (2021) was at age (>10) years old.**(Azza Shibl , 2021**), and in study in Indonesia was (1- 10) years old **(Swedish Childhood Cancer Foundation,2015).**

According to data collection we found the WBC count in our study is more than 10,000 /mm3 with rate of (41.7%) ,(5,000-10,000) /mm3 with rate of (33.3%) , while in a study in Indonesia, 90% of patients that had a relapse was less than 50,000/mm3.**(Swedish Childhood Cancer Foundation,2015)**.

Chapter seven
Conclusion & Recommendation

Conclusions :

Total Cases 106 had acute lymphoblastic leukemia, the most of them had B cells type of leukemia ,including (63.2%) were males, and (36.8%) were females. Most of these cases on regular treatment with rate of 89%, and 55% of cases were at high risk.

(11.3%) of Cases had a relapse, which including (7.5%) of cases with CNS relapse, (2.8%) of cases with hematological relapse, and only (0.9%) of case with testicular relapse. Most of relapseS were at (1-5) years of age, and with regard to sex, they wre equal between males and females.

Also most of relapses at high risk.

Recommendations:

1. We recommend doing further other researches comparing between two or more hospitals.

2. We recommend researches comparing between acute lymphoblastic leukemia and other types of leukemia.

3. We recommend the hospital administration to continuously communicate with patients to continue the treatment plan.

4. We recommend the doctors and medical staff to educate the patients about necessity of regular follow up in hospital.

5. We recommend the medical staff to document all information of patients.

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Appendix

Appendix (1):

Table (1) Characteristic of data according age in acute lymphoblastic patients , in Al-Kuwait Hospital Sana'a

Age	Frequency	Percent
1 year	1	0.9%
1 year, 6 month	3	2.8%
2 year,6 month	1	0.9%
2 years	8	7.5%
3 years	6	5.7%
4 years	15	14.2%
5 years	10	9.4%
6 years	12	11.3%
7 years	10	9.4%
8 years	11	10.4%
9 years	4	3.8%
10 years	5	4.7%
11 years	7	6.6%
12 years	4	3.8%
13 years	7	6.6%
16 years	2	1.9%
Total	**106**	**100%**

Appendix 2:

Table 3: Date of discovered disease :

Date	Frequency	Percent	Valid Percent	Cumulative Percent
10.01.20	1	.9	.9	.9
11.01.20	1	.9	.9	1.9
02.02.20	1	.9	.9	2.8
06.02.20	1	.9	.9	3.8
11.02.20	1	.9	.9	4.7
13.02.20	1	.9	.9	5.7
18.02.20	2	1.9	1.9	7.5
25.02.20	2	1.9	1.9	9.4
02.03.20	1	.9	.9	10.4
16.03.20	1	.9	.9	11.3
18.03.20	1	.9	.9	12.3
21.03.20	1	.9	.9	13.2
01.04.20	1	.9	.9	14.2
02.04.20	1	.9	.9	15.1
08.04.20	1	.9	.9	16.0
14.04.20	1	.9	.9	17.0
22.04.20	1	.9	.9	17.9
24.04.20	1	.9	.9	18.9
02.05.20	1	.9	.9	19.8
10.05.20	2	1.9	1.9	21.7
12.05.20	1	.9	.9	22.6
19.05.20	1	.9	.9	23.6
09.06.20	1	.9	.9	24.5
10.06.20	1	.9	.9	25.5
13.06.20	1	.9	.9	26.4
15.06.20	1	.9	.9	27.4
20.06.20	1	.9	.9	28.3
06.07.20	2	1.9	1.9	30.2
09.07.20	1	.9	.9	31.1
12.07.20	1	.9	.9	32.1
01.08.20	1	.9	.9	33.0
03.08.20	1	.9	.9	34.0
22.08.20	1	.9	.9	34.9
26.08.20	1	.9	.9	35.8
30.08.20	1	.9	.9	36.8
05.09.20	1	.9	.9	37.7
10.09.20	1	.9	.9	38.7
15.09.20	1	.9	.9	39.6

Date	Frequency	Percent	Valid Percent	Cumulative Percent
19.09.20	1	.9	.9	40.6
28.09.20	1	.9	.9	41.5
30.09.20	1	.9	.9	42.5
06.10.20	1	.9	.9	43.4
28.10.20	1	.9	.9	44.3
02.11.20	1	.9	.9	45.3
17.11.20	1	.9	.9	46.2
26.11.20	1	.9	.9	47.2
30.11.20	1	.9	.9	48.1
03.12.20	1	.9	.9	49.1
07.12.20	1	.9	.9	50.0
30.12.20	1	.9	.9	50.9
26.01.21	2	1.9	1.9	52.8
27.01.21	1	.9	.9	53.8
10.02.21	1	.9	.9	54.7
13.02.21	1	.9	.9	55.7
27.02.21	1	.9	.9	56.6
02.03.21	1	.9	.9	57.5
20.03.21	1	.9	.9	58.5
22.03.21	1	.9	.9	59.4
23.03.21	1	.9	.9	60.4
06.04.21	1	.9	.9	61.3
15.04.21	1	.9	.9	62.3
16.04.21	1	.9	.9	63.2
22.04.21	1	.9	.9	64.2
05.05.21	1	.9	.9	65.1
06.05.21	1	.9	.9	66.0
10.05.21	1	.9	.9	67.0
25.05.21	1	.9	.9	67.9
31.05.21	1	.9	.9	68.9
02.06.21	1	.9	.9	69.8
13.06.21	1	.9	.9	70.8
14.06.21	1	.9	.9	71.7
19.06.21	1	.9	.9	72.6
29.06.21	1	.9	.9	73.6
03.07.21	1	.9	.9	74.5
06.07.21	2	1.9	1.9	76.4
07.07.21	1	.9	.9	77.4
13.07.21	1	.9	.9	78.3
14.07.21	1	.9	.9	79.2
26.07.21	1	.9	.9	80.2
01.08.21	1	.9	.9	81.1

Date	Frequency	Percent	Valid Percent	Cumulative Percent
06.08.21	1	.9	.9	82.1
15.08.21	1	.9	.9	83.0
16.08.21	1	.9	.9	84.0
29.08.21	1	.9	.9	84.9
13.09.21	1	.9	.9	85.8
15.09.21	1	.9	.9	86.8
17.09.21	1	.9	.9	87.7
22.09.21	1	.9	.9	88.7
30.09.21	1	.9	.9	89.6
08.10.21	1	.9	.9	90.6
11.10.21	1	.9	.9	91.5
13.10.21	1	.9	.9	92.5
23.10.21	1	.9	.9	93.4
27.10.21	2	1.9	1.9	95.3
28.10.21	1	.9	.9	96.2
31.10.21	1	.9	.9	97.2
09.11.21	1	.9	.9	98.1
17.11.21	1	.9	.9	99.1
25.12.21	1	.9	.9	100.0
Total	106	100.0	100.0	

APPENDIX (3):

Table (3) Symptoms at early onset of diagnosis

Symptoms at early onset of diagnosis	Frequency	Percent	Valid Percent	Cumulative Percent
Abdominal distention , fever	1	.9	.9	.9
Abdominal distention	1	.9	.9	1.9
Abdominal distention & fever	1	.9	.9	2.8
Abdominal distention & HSM& decrease appetite	1	.9	.9	3.8
Abdominal distention & petechial rash	1	.9	.9	4.7
Abdominal distention &Lymphadenopathy	1	.9	.9	5.7
back pain	1	.9	.9	6.6
Back pain & fever for 3 months - epistaxis	1	.9	.9	7.5
bleeding	1	.9	.9	8.5
Bone pain	2	1.9	1.9	10.4
Bone pain , fever , loss of weight , loss of appetite	1	.9	.9	11.3
bone pain ,fever ,epistaxis	1	.9	.9	12.3
Bone pain & abdominal pain	1	.9	.9	13.2
bone pain, arthritis	1	.9	.9	14.2
Cervical & inguinal mass	1	.9	.9	15.1
Cervical and Neck L.N swelling, fever & dyspnea	1	.9	.9	16.0
cervical L.N swelling	1	.9	.9	17.0
Fatigue , abdominal distention	1	.9	.9	17.9
fever	2	1.9	1.9	19.8
Fever	6	5.7	5.7	25.5
Fever , abdominal distention , easy fatigability	1	.9	.9	26.4
Fever , bone pain	1	.9	.9	27.4
Fever , cough	1	.9	.9	28.3
Fever , vomiting	1	.9	.9	29.2
Fever ,decrease of weight ,pallor, fatigue	1	.9	.9	30.2
fever ,multiple swelling	1	.9	.9	31.1
fever ,pallor ,bone pain	1	.9	.9	32.1
Fever ,Pallor ,Petechia	1	.9	.9	33.0
Fever & back ulcer	1	.9	.9	34.0
Fever & bone pain	2	1.9	1.9	35.8
Fever & bone pain &abdominal pain	1	.9	.9	36.8
Fever & bone ache & decrease appetite &decrease body weight & fatigability	1	.9	.9	37.7

Table (3) Symptoms at early onset of diagnosis

Symptoms at early onset of diagnosis	Frequency	Percent	Valid Percent	Cumulative Percent
Fever & bone ache & lower limb swelling	1	.9	.9	38.7
Fever & headache	1	.9	.9	39.6
Fever & lethargy	1	.9	.9	40.6
Fever & pallor	1	.9	.9	41.5
fever & pallor & fatigue	1	.9	.9	42.5
Fever & skin ecchymosis & pallor	1	.9	.9	43.4
fever &abdominal distension	1	.9	.9	44.3
Fever &bone pain	1	.9	.9	45.3
fever &diarrhea & bone ache	1	.9	.9	46.2
fever &epistaxis	1	.9	.9	47.2
Fever &epistaxis &lethargy	1	.9	.9	48.1
fever &general fatigue	1	.9	.9	49.1
fever &HSM	1	.9	.9	50.0
fever &lethargy &pallor	1	.9	.9	50.9
Fever &pallor & bone pain	1	.9	.9	51.9
fever and body ache	1	.9	.9	52.8
fever and cough	1	.9	.9	53.8
fever and fatigability	1	.9	.9	54.7
fever and generalized bone ache	1	.9	.9	55.7
Fever, bone pain & axillary L.N swelling	1	.9	.9	56.6
Fever, bone pain, epistaxis & pallor	1	.9	.9	57.5
fever, diarrhea, abdominal distension, pallor, weight loss of appetite	1	.9	.9	58.5
fever, diarrhea, vomiting, abdominal pain	1	.9	.9	59.4
fever, epistaxis, bone pain	1	.9	.9	60.4
fever, fatigability and bone pain	1	.9	.9	61.3
fever, generalized body ache, neck swelling	1	.9	.9	62.3
fever, neck swelling	1	.9	.9	63.2
fever, pallor, hepatosplenomegaly	1	.9	.9	64.2
fever, abdominal pain, bone ache, fatigue	1	.9	.9	65.1
fever, bone pain	1	.9	.9	66.0
Fever ,fatigue , abdominal pain	1	.9	.9	67.0
fever, knee & joint pain and easy fatigability	1	.9	.9	67.9
fever. Abdomen distension and bone ache	1	.9	.9	68.9
fever& epistaxis	1	.9	.9	69.8
Fever& pallor	1	.9	.9	70.8
Fever & sore throat	1	.9	.9	71.7
Fever & fatigue	1	.9	.9	72.6
Headache & dyspnea	1	.9	.9	73.6
high grade fever	1	.9	.9	74.5
High grade fever & Abdominal . distention	1	.9	.9	75.5
High grade fever, easy fatigability	1	.9	.9	76.4
High grade fever, neck swelling & epistaxis	1	.9	.9	77.4
Joint pain ,skin rash	1	.9	.9	78.3

Table (3) Symptoms at early onset of diagnosis

Symptoms at early onset of diagnosis	Frequency	Percent	Valid Percent	Cumulative Percent
L.L bone pain ,back pain ,fever ,epistaxis ,melena	1	.9	.9	79.2
Multiple neck swelling & fever & sweating	1	.9	.9	80.2
multiple swelling	1	.9	.9	81.1
multiple swelling in neck &fever& decrease body weight &decrease appetite	1	.9	.9	82.1
Neck mass	1	.9	.9	83.0
neck swelling	1	.9	.9	84.0
Neck swelling	2	1.9	1.9	85.8
neck swelling ,fever ,loss of appetite	1	.9	.9	86.8
neck swelling and fever	1	.9	.9	87.7
neck swelling anemia	1	.9	.9	88.7
neck swelling, difficulty of walking	1	.9	.9	89.6
Pale , fever , fatige	1	.9	.9	90.6
pale & easy fatigue	1	.9	.9	91.5
Pale, easy fatigue, bone pain & Fever for 1 month	1	.9	.9	92.5
pale, fatigue, lymph nodes enlargement	1	.9	.9	93.4
Pallor, bone pain, fever & blood transfusion	1	.9	.9	94.3
pallor, fever, bone pain	1	.9	.9	95.3
pallor, right leg pain, petechial rash	1	.9	.9	96.2
Sore throat & fever	1	.9	.9	97.2
Sub mandibular swelling	1	.9	.9	98.1
Sudden anemia & pallor	1	.9	.9	99.1
Unable to walk & fever for 3 months - blood transfusion 1 month ago	1	.9	.9	100.0
Total	106	100.0	100.0	

APPENDIX (4):

Characteristic of data of all demographic variables per relapse:

Age Category

Relapse			Frequency	Percent	Valid Percent	Cumulative Percent
No Relapse	Valid	1-5 Years	36	38.3	38.3	38.3
		6-10 Years	40	42.6	42.6	80.9
		11-16 Years	18	19.1	19.1	100.0
		Total	94	100.0	100.0	
Yes Relapse	Valid	1-5 Years	8	66.7	66.7	66.7
		6-10 Years	2	16.7	16.7	83.3
		11-16 Years	2	16.7	16.7	100.0
		Total	12	100.0	100.0	

Sex

Relapse			Frequency	Percent	Valid Percent	Cumulative Percent
No Relapse	Valid	Male	61	64.9	64.9	64.9
		Female	33	35.1	35.1	100.0
		Total	94	100.0	100.0	
Yes Relapse	Valid	Male	6	50	50	50
		Female	6	50	50	100.0
		Total	12	100.0	100.0	

Duration

Relapse			Frequency	Percent	Valid Percent	Cumulative Percent
No Relapse	Valid	after induction	94	100.0	100.0	100.0
Yes Relapse	Valid	after induction	9	75.0	75.0	75.0
		no response	3	25.0	25.0	100.0
		Total	12	100.0	100.0	

Regular or irregular treatment

Relapse			Frequency	Percent	Valid Percent	Cumulative Percent
No Relapse	Valid	Regular	87	92.6	92.6	92.6
		Irregular	7	7.4	7.4	100.0
		Total	94	100.0	100.0	
Yes Relapse	Valid	Regular	7	58.3	58.3	58.3
		Irregular	5	41.7	41.7	100.0
		Total	12	100.0	100.0	

Available medication in each time

Relapse			Frequency	Percent	Valid Percent	Cumulative Percent
No Relapse	Valid	Not Available	9	9.6	9.6	9.6
		Available	85	90.4	90.4	100.0
		Total	94	100.0	100.0	
Yes Relapse	Valid	Not Available	1	8.3	8.3	8.3
		Available	11	91.7	91.7	100.0
		Total	12	100.0	100.0	

Type of risk

Relapse			Frequency	Percent	Valid Percent	Cumulative Percent
No Relapse	Valid	High Risk	50	53.2	53.2	53.2
		Low Risk	44	46.8	46.8	100.0
		Total	94	100.0	100.0	
Yes Relapse	Valid	High Risk	8	66.7	66.7	66.7
		Low Risk	4	33.3	33.3	100.0
		Total	12	100.0	100.0	

WBC count

Relapse			Frequency	Percent	Valid Percent	Cumulative Percent
No Relapse	Valid	Less than 5	39	41.5	41.5	41.5
		5-10	17	18.1	18.1	59.6
		above than 10	38	40.4	40.4	100.0
		Total	94	100.0	100.0	
Yes Relapse	Valid	Less than 5	5	41.7	41.7	41.7
		5-10	3	25.0	25.0	66.7
		above than 10	4	33.3	33.3	100.0
		Total	12	100.0	100.0	

RESEARCH FORM

Name ……..Age……...Gender……City…….
Type of leukemia……..
Date of discover the disease……
Symptoms at early onset of disease: …… ……..
Type of risk: ……WBC count…….
Flowcytometry……
Treatment: Duration of treatment…….
Type of relapse…… Time of relapse……....

استمارة بحث

الاسم ..... الجنس ..... العمر ..... المدينة .....
نوع سرطان الدم ..... نوع ابيضاض الدم البيضاء هل خلايا تائية او بائية .....
تاريخ اكتشاف المرض .....
الأعراض في بداية المرض .....
درجة الخطورة ..... عدد كريات الدم البيضاء .....
العلاج: ..... مدة العلاج: .....
نوع الانتكاسة ..... وقت الانتكاسة .....

الخلاصة

الانتكاسة عند الأطفال المصابين بابيضاض الدم الليمفاوي الحاد

في مركز سرطان الدم بمستشفى الكويت خلال2020-2021

الخلفية: يعد سرطان الدم الليمفاوي الحاد سرطانًا يصيب خط الخلايا اللمفاوية في الدم والذي يتميز بتطور عدد كبير من الخلايا اللمفاوية غير الناضجة. ويعد سرطان الدم السرطان الأكثر شيوعاً بين الأطفال والكبار اليمنيين. يتم علاج معظم حالات سرطان الدم بواسطة العلاج الكيميائي، وخلال هذه الحالات يمكن حدوث انتكاسة ، ونظراً لأن الجهاز العصبي المركزي هو موقع شائع للانتكاسة في سرطان الدم الليمفاوي الحاد، فإن بحثنا يستهدف دراسة الانتكاسة بين المرضى المصابين بسرطان الدم الليمفاوي الحاد.

الهدف: يهدف البحث إلى تحديد الانتكاسة التي تحدث بين المرضى المصابين بسرطان الدم الليمفاوي الحاد في مركز سرطان الدم لمستشفى الكويت الجامعي بمدينة صنعاء في الفترة من 1 يناير 2020 إلى 31 ديسمبر 2021.

المنهجية: تم إجراء دراسة وصفية استرجاعية على الأطفال المصابين بسرطان الدم الذين تم علاجهم في وحدة سرطان الدم في مستشفى الكويت الجامعي بمدينة صنعاء. حيث تضمنت عينة الدراسة 106 طفلاً تم تشخيصهم بالسرطان في مركز سرطان الدم في مستشفى الكويت الجامعي بمدينة صنعاء في الفترة من 1 يناير 2020 إلى 31 ديسمبر 2021، تم جمع البيانات من الملفات وتحليلها باستخدام SPSS .

النتائج: من أصل 106 حالة من الأطفال المصابين بسرطان الدم الليمفاوي الحاد الذين حدث لديهم انتكاسة، كان هناك 12 حالة فقط، بنسبة (11.3٪) من عينة البحث، وكان لدى ثمانية منهم انتكاسه المرض في الجهاز العصبي المركزي، وثلاثة منهم كانت انتكاسة المرض في الجهاز الدموي، وكان لدى حالة واحدة فقط انتكاسه المرض في الخصية.

في انتكاسة الجهاز العصبي المركزي: خمس حالات في مجموعة الأعمار (1-5) سنوات بنسبة (62.5٪)، حالة واحدة في مجموعة الأعمار (6-10) سنوات بنسبة (12.5٪)، وحالتان في مجموعة الأعمار (11-16) سنة بنسبة (25٪) , وفي انتكاسه المرض في الجهاز الدموي: حالتان في مجموعة الأعمار (1-5) سنوات بنسبة (66.7٪) من الحالات المتأثرة بانتكاسه المرض، بنسبة (4.5٪)، وحالة واحدة فقط من انتكاسه المرض في مجموعة الأعمار (6-10) سنوات بنسبة (33.3٪)، ولم تحدث أي حالات انتكاسة في الجهاز الدموي في مجموعة الأعمار (11-16) سنوات , إما في انتكاسه المرض في الخصية، كانت هناك حالة واحدة فقط من هذا النوع من انتكاسه المرض، بنسبة (100٪)، في مجموعة الأعمار (6-10) سنوات.

الاستنتاجات: كانت هناك 106 حالات من الأطفال المصابين بسرطان الدم الليمفاوي الحاد، وكان معظمهم من نوع خلايا B، بنسبة (63.2٪) من الذكور، و (36.8٪) من الإناث . كان 55٪ من الحالات على مستوى عالٍ من المخاطر. كانت (11.3٪) من الحالات تعاني من انتكاسه المرض، بما في ذلك (7.5٪) من الحالات في الجهاز العصبي المركزي، و (2.8٪) من الحالات في الجهاز الدموي، وحالة واحدة فقط بانتكاسه المرض في الخصية بنسبة (0.9٪). وكانت معظم حالات انتكاسه المرض في الفئة العمرية (1-5) سنوات، وبالنسبة للجنس، كانت متساوية بين الذكور والإناث.

الكلمات المفتاحية: سرطان الدم، الانتكاسة . سرطان الدم الليمفاوي الحاد