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A comparative Study of Survival to MSK in pediatric leukemia Based Study of Individual Data for 300 Children in Iraq

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Abstract: This paper aims to make a comparative study of survival to MSK in pediatric leukemia based study of individual data for 300 children in Iraq.A retrospective study was conducted in different hospitals in Iraq where all medical records from 20-1-2019 to 4-2-2022 were reviewed for children under the age of 14 years as 300 children were included in this study, distributed in two groups (No MSK involvement, 200 children, and MSK involvement 100 children. Data and demographic information about children suffering from Lekima were collected from different hospitals in Iraq, where the data was designed and collected in this retrospective study by collecting 300 children distributed into two groups. Patients' information, including blood preparation, blood chemistry, ALL, and the year of diagnosis, were recorded. immunophenotyping of cell surface markers was additionally used to differentiate subtypes (i.e., AML from ALL, and T-cell ALL from B-cell ALL) Risk classification was based on NCL of patients aged 1 to 14 years and was enrolled WBC values less and higher than 109 * 50 Of 300 childhood leukemia cases, 100 (33.3 %) children had MSK involvement at initial presentation. MSK involvement was more likely in children with acute lymphoblastic leukaemia than acute myeloid leukemia ($p < 0.05$).Hematologic abnormalities were less frequent in the MSK involvement group ($p < 0.05$). The absence of peripheral blast cells was significantly higher in the MSK involvement group.

Keywords: Abnormalities, MSK, leukaemia, diagnosis, children.

INTRODUCTION

Leukemia in children (leukemia) is a malignant disease of the blood, which is accompanied by a violation of blood formation in the bone marrow, as well as the replacement of normal blood cells by immature blast cells of the leukocyte series. The incidence of leukemia in children is 4-5 cases per 100,000 children.

Statistics show that leukemia is the most common type of childhood cancer (30%). Most often, leukemia is diagnosed in children between the ages of two and five years [Bidwell, S.S. *et al*., 2019; Steliarova-Foucher, E. *et al*., 2017; Clarke, R.T. *et al*., 2016].

It has been proven that acute leukemia is a "clonal" disease. As a result of the mutation process that occurs in the hematopoietic cell, its differentiation occurs in the stage of immature forms (blasts) with its further growth (proliferation). A malignant tumor forms that replaces the bone marrow and interferes with normal blood formation [Kai, T. *et al*., 1996; Barbosa, C.M. *et al*., 2002]. The blasts begin to leave the bone marrow, enter the bloodstream, and spread throughout the body—the development of leukemic infiltration in organs and tissues [Kobayashi, D. *et al*., 2005; Robazzi, T.C.M.V. *et al*., 2007].

The causes of chromosome breakage are diverse and consist of genetic predisposition and exogenous and endogenous factors. It has been shown that ionizing radiation, chemicals, viruses and bacteria [Sinigaglia, R. *et al*., 2008], and genetic predisposition (hereditary syndromes with an abnormal number of chromosomes, defects in genes) can play a role in leukemia [Biswas, S. *et al*., 2009; Zombori, L. *et al*., 2013; Riccio, I. *et al*., 2013]. Among these factors, the most common is Down syndrome, in which the risk of developing RA is about 20 times higher than that of children without this syndrome [Tsujioka, T. *et al*., 2018].

The diagnosis of ALL is established if there are more than 20% of blasts in the bone marrow perforation. According to the morphological criteria of blast cells, ALL has three types: L1 (85% of patients), L2 (14%), and L3 (1%) [Maman, E. *et al*., 2007].

The clinical picture of ALL is determined by the degree of infiltration of the bone marrow by blast cells and the extramedullary spread of the process [Brix, N. *et al*., 2015; Tragiannidis, A. *et al*., 2016].

In the clinical course of ALL, the following periods are distinguished: pre-leukemic, acute, remission, relapse, and end.

The clinical manifestations of ALL depend on the nature of clonal leukemia, the timing of diagnosis, and the timing of treatment initiation [Jonsson, O.G. *et al*., 1990].

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In the initial stage of the disease (pre-leukemic period), nonspecific symptoms may occur: increased body temperature, decreased appetite, increased weakness, increased fatigue, and lethargy. In the study of peripheral blood, anaemia, agranulocytosis, and thrombocytopenia can be detected (but not always). Often, these changes are documented in the study of the bone marrow [Kang, S. *et al*., 2017].

The acute period is characterized by symptoms of intoxication, loss of appetite, bone pain, an increase in anaemia, and the appearance of the hemorrhagic syndrome (from petechiae and hematomas to various bleeding: nasal, gastrointestinal, renal) [Smith, M. *et al*., 1996]. One of the frequent symptoms is an increase in the peripheral lymph nodes - submandibular, cervical, axillary, and inguinal. They are painless, mobile, and not welted to each other and surrounding tissues [Laosombat, V. *et al*., 2002]. Enlargement of the liver and spleen is characteristic. Ulcerative-necrotic lesions of the mucous membranes in the form of gingivitis, stomatitis, and enteropathy occur due to leukemic infiltration with bleeding and infection [Tubergen, D.G. *et al*., 1993].

MATERIAL AND METHOD

Patient Sample

A retrospective study was conducted in different hospitals in Iraq where all medical records from 20-1-2019 to 4-2-2022 were reviewed for children under the age of 14 years as 300 children were included in this study, distributed in two groups (No MSK involvement, 200 children, and MSK involvement 100 children

Study Design

Data and demographic information about children suffering from Lekima were collected from different hospitals in Iraq, where the data was designed and collected in this retrospective study by collecting 300 children distributed into two groups.

Patients' information, including blood preparation, blood chemistry, ALL, and the year of diagnosis, were recorded.

immunophenotyping of cell surface markers was additionally used to differentiate subtypes (i.e., AML from ALL, and T-cell ALL from B-cell ALL)

Risk classification was based on the NCL of patients aged 1 to 14 years and was enrolled with WBC values less than 109 * 50

Study Period

An agreement was made with the relevant committees in order to obtain the required licenses for this study, as the study period was for a full year and included following up on developments in addition to monitoring the patient and This study started from 20-1-2019 to 4-2-2022.

Aim of Study

This paper aims to make a comparative study of survival to MSK in pediatric leukemia based study of individual data for 300 children in Iraq.

RESULTS

Table 1: Demographic results of patients

Variable	No MSK involvement	MSK involvement
Age		
5-9	120	70
10-14	80	30
Sex		
B	111	64
G	89	34
Morphology		
ALL	130	60
AML	70	40
ALL subtype		
B-cell	99	40
T-cell	56	30
FAB classification	50	30
Symptoms		
Fever	140	70
Skin bleeding	120	30
Hepatomegaly	88	16

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Splenomegaly	102	14
Lymphadenopathy	103	10
Risk groups for childhood		
The WBC count is less than 50,000 cells/mm3 (50.0 x 10^9 cells/L).	110	44
WBC count is greater than 50,000 cells/mm3 (50.0 x 10^9 cells/L)	90	56
Platelets, $\times 10^9$ /L		
<100	95	56
≥100	105	44

Table 2: Distribution of patients according to Blasts in peripheral blood

P	G1	G2
Absence	9	8
Presence	191	92
Calcium, mg%	9.3%	9.7%
Phosphate, mg%	5.1%	5.2%
ALP, U/L MEAN ±SD	135±40.7	119±45.6
LDH, U/L MEDIAN	1189 (711-2234)	989(711-2123)
LDH, U/L		
<500	55	32
≥500	145	68

Table 3: Distribution of patients according to Time period of diagnosis

	No MSK involvement	MSK involvement	P value
2019-2020	90	40	0.05
2020-2021	50	40	0.45
2021-2022	60	20	0.01

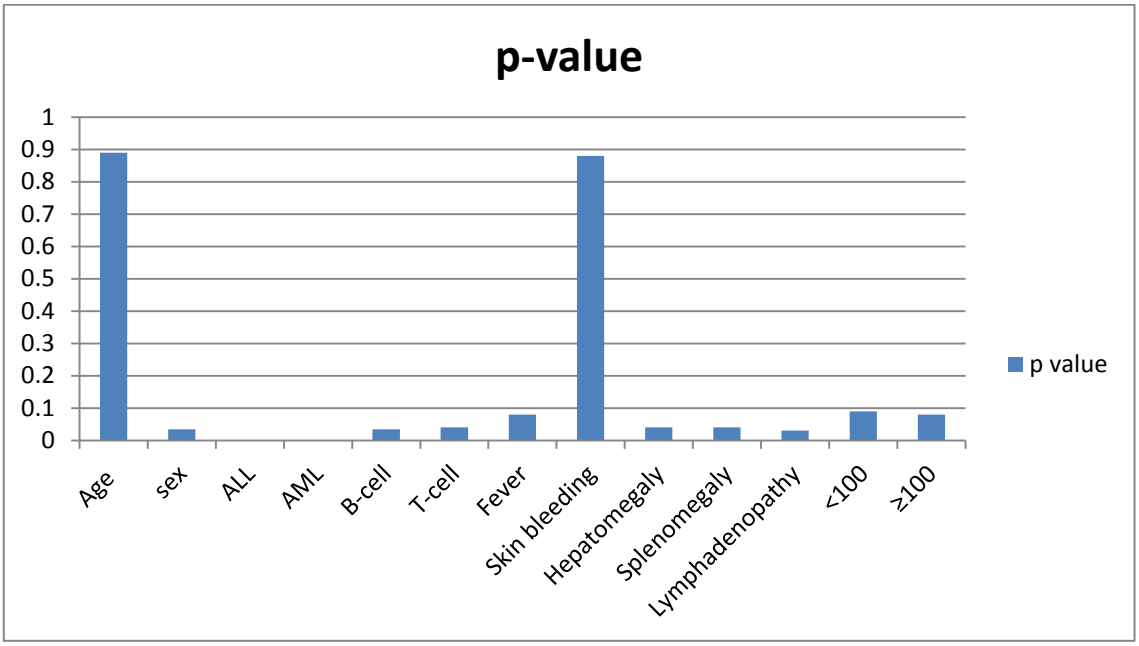

Figure 1: P-value of results

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Table 4: Treatment Results of the patient according to Risk groups for childhood

Death	Slandered	High	P value
All	2	4	0.03
Complication	1	2	0.87
Other reason	----	2	0.01

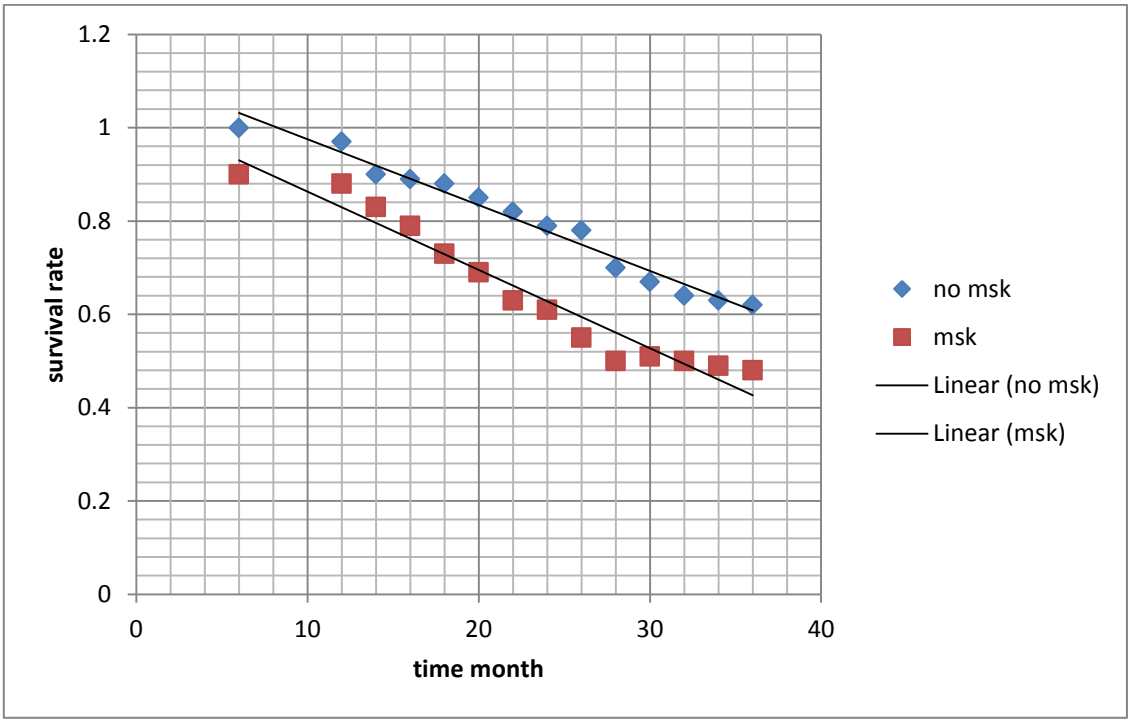

Figure 2: Disease-free survival rates

Table 5: Comparison of overall survival by musculoskeletal involvement among the 300 propensity-score matched study patients

	0	12	24	36
NO MSK	150	45	18	0
MSK	70	28	5	0

DISCUSSION

300 patients were collected from the hospital and distributed into two groups (no 200 patients and 100 patients for the MSK group).

were distribution of patients according to sex into a group with No MSK involvement (120 boys and 80 girls, and a group of MSK involvement, 64 Males and 34 females, the most frequent symptoms were fever for 140 patients and skin bleeding For 120 patients, the least frequent and prevalent symptoms in patients were hepatomegaly for 88 patients, as for the MSK involvement group, the most frequent symptoms were fever for 70 patients and skin bleeding for 30 patients, while for the least frequent symptoms were lymphadenopathy for ten patients.

Patients were distributed according to risk groups for childhood, where the WBC count was less than 50,000 cells/mm3 (50.0 x 109 cells/L for 110 patients). As for the MSK involvement were 44 patients.

(WBC count is greater than 50,000 cells/mm3 (50.0 x 109 cells/L) for 90 patients and the 56 MSK involvement group, and a statistically significant relationship between the variables was found at a 0.01 p-value.

Reported a lower incidence of MSK involvement in childhood leukemia than these previous studies reporting only cases with bone and/or joint pain. The explanation may be differences in the definitions, as apart from bone and joint complaints, most of the cases in our study had radiologic evidence of bone and joint involvement. In comparison, the studies which included subjective MSK complaints tended to report higher incidences of MSK involvement. Riccio et al. [Riccio, I. *et al.*, 2013] retrospectively reviewed 328 childhood leukemia cases and reported that

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22.3% of their cases had MSK symptoms, while Robazzi et al. reported that 54.7% of 406 childhood leukemia patients had osteoarticular manifestations [Robazzi, T.C.M.V. *et al*., 2007].

Despite the fact that OL in children over one year of age is divided into lymphoma (ALL) and myeloid (AML), this classification is not very clear in OL in children under one year of age since cases of transformation are from one type of OL To another was described. In HAPE, blastocysts and lymphocytic leukemia have similar immunological and genetic alterations, and a mixed immunophenotype or signs of undifferentiated leukemia are observed, which greatly complicates the diagnosis. These biological features of HAPE indicate the neoplastic transformation of early progenitor cells that have not yet fully committed to lymphoid and/or myeloid differentiation.

The clinical manifestations of acute myelogenous leukemia (AML) and ALL in children younger than five years of age are similar and are leukocytosis, damage to the central nervous system (in 14% of cases), skin (in the form of thick bluish or red nodules) [Steliarova-Foucher, E. *et al*., 2017], enlargement of the liver and spleen. The disease can present for the first time with clinical manifestations of meningitis, encephalitis (due to damage to the central nervous system), and hyperbilirubinemia. Congenital leukemia must be differentiated from CMV infection, hepatitis, and sepsis [Bidwell, S.S. *et al*., 2019; Clarke, R.T. *et al*., 2016; Kobayashi, D. *et al*., 2005; Biswas, S. *et al*., 2009] Due to anemia syndrome

CONCLUSION

Our study found that joint pain was the most common MSK involvement, and the large joints of the extremities, especially the ankles and knees, were the most commonly involved sites. This clinical characteristic of MSK involvement was similarly reported in previous studies.

The polyarticular joint pain pattern was the most common presentation in our study, which was similar to a study by Spilberg and Meyer. However, most previous studies found that the oligoarticular pattern was the most common presentation.

RECOMMENDATION

In patients with leukemia, the proper maturation of the hematopoietic cells does not occur, and the blood produces too many leukemic cells.

For chronic leukemia, the 5-year survival rate is less beneficial because children can live with leukemia for a long time without actual treatment. In the past, 5-year survival rates were 60-80%, but now they are much higher.

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