JKBMS, Vol.6, No.1, P.22-27, 2020 https://doi.org/10.56056/amj.2020.114

Demographic and pattern of childhood acute leukemia in Duhok, Kurdistan region of Iraq, 2009-2018

Adnan Anwer Sedeeq AL-doski*

Abstract

Background and objectives: Leukemia is a common childhood cancer, constituting more than 25% in many populations. The most frequent type of childhood leukemia is acute lymphoblastic leukemia. The aim of this study is to describe the annual incidence, rate and demographics of acute childhood leukemia and their patterns in Duhok, Kurdistan - Iraq, in the period from 2009 to 2018. **Methods:** It is a retrospective study that was conducted at Heevi Pediatric Teaching Hospital in Duhok. A total of 198 patients, who were diagnosed as new cases of acute leukemia and were less than 15 years of age in the past ten years (from 2009 to 2018), were included in this study. Demographic data and the presenting hematological values of acute leukemia, based on cytomorphologic characteristics of bone marrow leukemic blast cells, were studies. **Results:** Childhood acute leukemia represented about 40 % of the total percentage of cancers among children in Duhok. It was more predominant in boys (53.5%) than in girls (46.5%). The cases peaked at 2-10 years cohort (69.2%). The number of cases ranged from 17 cases in 2009 to 15 cases in 2018 and reached a peak of 31 cases in 2016. The most prevalent type of leukemia was Acute Lymphoblastic Leukemia (ALL) (161 cases, 81.6%), followed by Acute Myeloid Leukemia (37 cases, 18.4%). The overall annual incidence rate was 2.0 cases /100,000 per year. The yearly incidence rates of leukemia were 1.3 – 2.4 cases /100,000. The highest incidence rate was in Duhok center (2.4 cases /100,000) and Zakho (2.3 cases /100,000); however, the least incidence rate was in Amedi (1.3 cases /100,000). The incidence of ALL appears to be nearly fourfold higher than the incidence of Acute Myeloid Leukemia in different areas of Duhok. **Conclusions:** It was found that childhood acute leukemia had lower prevalence in Duhok, and the clinical hematological features were similar to that of other studies.

Key words: Acute leukemia, Childhood, Duhok, Incidence rate.

Introduction

Acute leukemia is a heterogeneous entity of cancer, which results from clonal proliferation blasts (either lymphoblasts or myeloblasts) and infiltrates different tissues. There are different types of leukemia with various demographic and geographical distributions. Acute Lymphoblastic Leukemia (ALL) constituted about 80% of leukemia in children aged 0 – 15 years[1]. The incidence of childhood leukemia shows higher rates in resource-rich countries, ranging from 4.0 to 4.4 per 100,000/year[2] (e.g., 4.0 cases per 100,000 children among industrialized western European countries)[3;] however, the incidence is lower in less-developed countries (e.g., 0.9 case per 100,000/year in Vietnam)[2].

In developed countries, the precursor B-cell subtype constitutes about 80% of ALL, therefore, it is responsible for the peak of incidence in early childhood and the obvious variation of childhood leukemia among different populations[4,5]. The second most common type of leukemia in childhood is Acute Myeloid Leukemia (AML) In Europe, AML constitutes about 20% of childhood leukemia, and worldwide, the incidence is stable with a range of 0.5–1 case per 100,000/year[1,3]. The cause of childhood leukemia, in majority of cases, is unknown. In addition to the exposure to ionizing radiation during pregnancy and after birth, the genetic factor is a known suspected cause (2–3% of cases are related with Down syndrome)[6, 7]. Infectious diseases are possible to have a role in the cause of childhood leukemia, especially ALL[7, 8]. Delayed exposure to infection during early infancy could result in an abnormal response, leading to the development of leukemia. Unidentified infectious agent might be a rare specific response for leukemia. The environmental carcinogens can modify the risk

*M.B.Ch.B., F.I.B.M.S, Assistant professor, Department of Pathology, College of Medicine, University of Duhok, Duhok, Iraq. dr_adnananwar@uod.ac

of genetic susceptibility[9, 10]. There is a positive correlation between leukemia, particularly ALL with ecology, and increasing socioeconomic condition[11,12]. The causes for this are not clear. The aims of this study are to describe the incidence, pattern rate and demographic of acute childhood leukemia and their patterns in Duhok, Kurdistan Region of Iraq.

Patients and methods

Duhok is the third province in the Kurdistan region of Iraq. Heevi Pediatric Teaching Hospital is the main hospital for children in Duhok and the only available source of information. Heevi hospital had started data collection in 2009, and there were no accurate leukemia data record before.

This is a record study of 198 unselected childhood acute leukemia patients, aged 0 day-15 years, who were diagnosed in January 2009 - December 2018.

The diagnosis was based on blood film morphology of blast cells in peripheral blood and/or bone marrow, typed by the French-American-British (FAB) criteria. In the first two years, cytochemical test was used for confirmation; after that, all the cases were confirmed and classified by Immuno-phenotyping procedure. Cytogenetic and molecular facilities were performed for many cases, but were not included in the study. Standard criteria were used to diagnose leukemia. It was divided into ALL, with further division into subtypes B- or T- ALL, AML, and chronic leukemia, which was not included in the study and are very rare during childhood (only 2 cases of chronic myeloid leukemia and no cases of chronic lymphocytic leukemia were diagnosed during the period). Data concerning age, sex, area of residence, socioeconomic status, the presenting clinic-hematological findings, morphological subtypes and the annual incidence rate for geographical distribution were also determined and analyzed. The work was approved by the ethics committee of college of medicine – university of Duhok. All analyses were carried out with the Statistical Package for the Social Sciences (SPSS) software (Version 15.0). Chi-square test was used for categorical variables. Incidence data were reported for each year by dividing the incidence by the population (aged 0–15 years) for each year, then multiplying by 100,000.

Results

There were 198 new cases of childhood acute leukemia, with a median of 4.3 years and a range of 0 –15 years, registered in Duhok from 2009 to 2018. It represented about 40% of the total percentage of cancers among children in Duhok. The number of cases ranged from 17 cases in 2009 to 15 cases in 2018, and reached a peak of 31 cases in 2016; the annual incidence is 20 cases per year. The data showed that the incidence of leukemia was more in males (53.5%) than in females (46.5%), with a ratio of 1.15:1. A peak acute leukemia incidence was seen at the ages of 2-10 years (69.2%), Table 1.

Table (1): Demography of childhood acute leukemia occurrence in Duhok province from 2009–2018

Parameters	Total No. of cases	No. of cases Per year	Annual rate per 100,000 Inhabitants
Total new cases	198	20	2.0
Types		Cases	
B-ALL	146	73.7	1.49
T-All	15	7.6	0.14
AML	37	18.7	0.37
Gender			
Male	106	53.5	2.04
Female	92	46.5	1.77
Age (years)			
< 2	35	18.4	0.32
2- 9	136	67.2	1.24
≥ 10	27	14.4	0.25
Socio-economic classes	No	%	
Low	106	54	
Medium	72	36	
Good	20	10	

The diagnosis of patients throughout the years (31.8% in spring, 26.7 % in summer, 21.2% in winter, and 20.2% in autumn), according to the months, was the most frequent in August (24 cases), and least frequent in February (10 cases). The predominant type of acute leukemia in Duhok is ALL, 161 cases (81.6%), followed by AML, 37 cases (18.4%). The subtypes of ALL (146 cases, 90.7%, are B-ALL, and 15 cases, 9.3%, are T-ALL) were confirmed by immunophenotyping study (flow cytometry procedure). The hematological tests during diagnosis were as follow; mean Hb was 8.2 (±4.9) with a range of 3.5-19.8 g/dL, and the WBC count ranged from 0.7 to 749.2 x109/L, with a mean of 62.7 (±116.3). The mean platelets of the newly diagnosed acute leukemia were 71(±70) and the range was 6-434 x109/L. In 23.3 % of B-ALL & 37.8% of AML cases, the WBC count were > 50 x109/L, but highest T-ALL cases (80%), the WBC count were of > 50 x109/L, Table 2. The highest percentages of patients who were 2-9 years had B-ALL (110 cases 75.3%), those who were > 10 years had T-ALL (7 cases 46.7%), and those who were < 2 years had AML (12 cases 32.5%), Table 2. There were 3 cases of congenital acute leukemia, and in 16 cases the age of the patients was less than 1 year.

Table (2): Comparison of age and hematological parameters, between B-ALL, T-ALL and AML cases.

Characteristics		B-lineage ALL (n=146)		T-lineage ALL (n=15)		AML (n=37)		p-value
		No.	%	No.	%	No.	%	
Age years	Mean ±SD	5.1 ± 3.42		7.1 ± 4.82		5.6 ± 4.91		0.214
	(range)	(0.1–14)		(0.8–14)		(0.1–15)		
	< 2	21	14.4	2	13.3	12	32.5	< 0.001
	2- 9	110	75.3	6	40.0	17	45.9	
	≥ 10	15	10.3	7	46.7	8	21.6	
Hb Level	Mean ±SD	8.1±5.42		8.4 ± 1.76		8.4 ± 2.99		0.924
	(range)	(3.9–13.4)		(5.8–11.5)		(3.5–19.8)		
g/dl	< 9	119	81.5	11	73.3	26	70.3	0.175
	≥ 9	27	18.5	4	26.7	11	29.7	
WBC $\times 10^9$ /l	Mean ±SD	48.1 ± 10.4.9		159.9 ± 151.4		94.1 ± 132.2		0.001
	(range)	(0.7–746.2)		(12.1-518)		(0.7–495)		
	< 50	112	76.7	3	20	23	62.2	0.001
	≥ 50	34	23.3	12	80	14	37.8	
PLT $\times 10^9$ /l	Mean ±SD	68 ± 66		57 ± 378		91 ± 92		0.181
	(range)	(6-434)		(23-144)		(12–383)		
	< 50	49	33.6	8	53.3	22	59.5	0.149
	≥ 50	97	66.4	7	46.7	15	40.5	

There was a wide range of leukocyte counts at diagnosis, from very low to more than 700 x 109/L. In about 20% of children with ALL, the leukocyte counts were more than 50,000 x109/L. The significance of FAB morphological criteria, L1 was more than L2 in our patients, 68.3% and 27.9%, respectively. About the immunophenotyping classification of ALL, the most common phenotype was common B-ALL (cB-ALL), which constituted 77.6% of the cases. In T cell phenotype, 9 cases (5.6 %) were cortical T-ALL (table 3). Regarding AML, the most frequent subtype was AML-M2, which was reported in 13 cases (35.1%), and no cases of M6, M7 were found during the period of the study, Table 3.

Table (3): Lineage subtypes among childhood acute leukemia.

ALL	pro BALL	common BALL	pre-BALL	mature BALL	pro TALL	pre-TALL	cortical TALL	mature TALL	Total
Count	10	125	5	6	2	3	9	1	161
%	6.2%	77.6%	3.1%	3.7%	1.3 %	1.9%	5.6%	0.6%	100%
AML	**M0**	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**Total**
Count	4	8	13	3	4	5	0	0	37
%	10.8%	21.6%	35.1%	8.1%	10.8%	13.5%	0	0	100%

Childhood acute leukemia incidence rates in 91% of cases were reported in communities of low to medium socio-economic status, and only 9% of the cases were of high socio-economic status. During the period of the study, from January 2009 to December 2018, the annual incidence rate was 2.0 cases/100,000 per year, and the yearly incidence rates had a range of 1.3 – 2.4 cases /100,000, Figure 1.

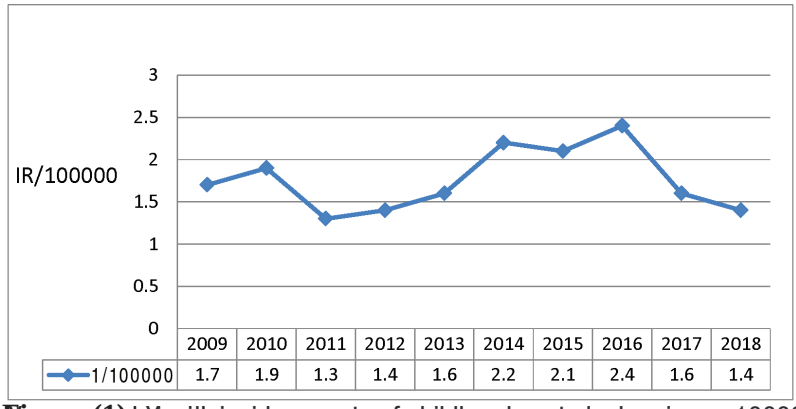

Figure (1): Yearly incidence rate of childhood acute leukemia per 100000 in Duhok.

As observed in Figure 2, in different districts in Duhok, the ten years crude incidence rates showed that the highest incidence rate was in the center of Duhok (2.4 cases per 100,000), followed by Zakho (2.3 cases per 100,000); however, the least incidence rate was observed in Amedi (1.3 cases per100,000). The incidence of ALL appears to be nearly fourfold higher than the incidence of AML in different areas of Duhok, Table 1.

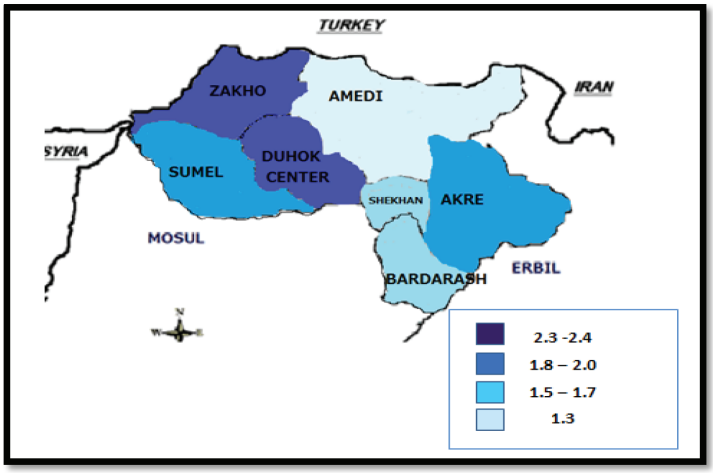

Figure (2): Geographical distribution of childhood acute leukemia average rates in various districts in Duhok (2009-2018)

Discussion

In Duhok, almost all childhood acute leukemia cases were diagnosed and registered in Heevi pediatric teaching hospital, and then referred to Jeen Hematology Center, which is responsible for the treatment of all childhood malignancies in Duhok province. The data show that the rates of leukemia in children aged 0 -15 years did not change during the period study; 198 cases of acute leukemia were diagnosed (20 cases per a year). In the present study, leukemia constitutes about 40% of pediatric cancers in Duhok, while international percentages show 35% in India and China, 33% in Germany, 30% in Ireland and France, and 27% in United States [13,14].

Regarding leukemia incidence in children in Duhok (2 per 100,000 per year), ALL and AML was 1.6 and 0.4 per 100,000 per year, respectively. The rate of leukemia of children <15 years old has been estimated in developed countries to be 4 per 100,000/year and in the developing countries to be 2.5 per 100,000/year[15, 16]. The average annual rate of all types of childhood leukemia did not noticeably rise in Duhok during the ten years of study, except for the peak in 2014-2016 (2.1-2.4/100,000 per year), which was due to displacement of a large number of refugees from Mosul area after the outbreak of the Islamic States in Iraq and Syria (ISIS).

The age distribution of childhood leukemia in Duhok has a peak between the ages of 2-9 years, the highest rates were 2-4 years (Mean 5.29 years, Median 4 years). It is the same in the United States and United Kingdom where the peak incidence occurs between ages of 2-5 years [17,18]. In Middle East, a study showed that the mean, median and range of age of children with ALL were 5.27, 4.27, and 0.2-14.5 years, respectively [19]. The rates of childhood leukemia subtypes (B-ALL, T-ALL, and AML) were not elevated and the predominant type was common B-ALL. This distribution was parallel to that studied in other countries[18, 20]. The gender distribution ratio of boys to girls is 1.15:1, which is similar to the United States where the ratio is 1.20:1. It has also been observed that in many developing countries, the incidence in boys is substantially higher than in girls in all age groups, except in infants where the more predominantly affected are females; these findings are almost universal[21,22]. The percentage of adolescent patients in our study (>10 years) was slightly higher than that reported in Saudi Arabia (13.5% vs.10.9%)3. Adolescents with ALL are usually present with adverse features at diagnosis, including T type ALL compare to B-ALL, higher presenting leukocyte count compare to B-ALL (mean WBC 160 vs. 48x109/L) [23, 24]. In the current study, childhood leukemia incidence revealed higher rates in the north of Duhok (Zakho) and the center of Duhok, in comparison to the east of Duhok city (Amedi and Akre). These two regions were exposed to great environmental pollution during recent decades. Zakho was exposed to many environmental carcinogens, such as depleted uranium from the last war and aromatic hydrocarbons (like benzene), which are known to be carcinogenic even at low levels[25,26]. The socio-economic statuses of our patients were of different classes: low, medium, and high; 40%, 51%, and 9%, respectively. There are some demographic studies about the association between leukemia and socio-economic status, and most of these studies showed a weak relationship between leukemia and high socio-economic status[27, 28]. Seasonal difference in the study was not significant, and there was no difference in the onset of the disease during different seasons of the year. It's comparable to a study of 15,855 cases with childhood leukemia that failed to reveal any proof of seasonality[29]. Pallor, lymph node adenopathy and splenomegaly were the common presenting features, and they were seen in 68 %, 59 % and, 48%, respectively, followed by bleeding tendency (30%) and hepatomegaly (26%). This is in contrast to features found in Saudi Arabia [19], and similar with findings in some Western countries in which enlargement of spleen and liver of children with ALL constituted (30-50%)[30]. We saw that some patients were misdiagnosed as connective tissue disorder (Rheumatoid disorders), Immune Thrombocytopenia Purpura (ITP) or anemia, and were given management accordingly. This misdiagnosis is due to inappropriate assessment of certain features of leukemia, such as fever, anemia, bleeding tendency and joint pain. This causes delay in transfer of such cases, disturbing treatment outcome and prognosis. The descriptives of hematological findings were similar to other studies; anemia and thrombocytopenia were most frequent features of childhood acute leukemia[31]. The percentage of cases with a leukocyte count above 50x109/L was higher than that seen in Saudi Arabia (30.3% vs.16.6%)[19]. The presenting peripheral blood leukocyte count is an important predictor of treatment outcome, with poor favor outcomes as the leukocyte count increases32. The significance of FAB morphological of L1 and L2 in this study was approximate to other studies, where L1 was the most frequent type (67.9% - 84%)[19, 33]. By treating patients with more intensive regimens, the FAB classification was not observed to be an important prognostic variable[34].

Conclusions

The patterns of childhood acute leukemia have the same characters as previous studies. The result indicated a lower annual incidence rate of childhood acute leukemia in Duhok. Further studies, including genetic molecular study and therapy related follow up, are important in order to create better plans to deal with cancer.

Reference

1. Terwilliger T, Abdul-Hay M. Acute lymphoblastic leukemia: a comprehensive review and 2017 update. Blood Cancer J 2017; 7(6), e577. http://doi.org/10.1038/bcj.2017.53.

2. Forman D, Bray F, Brewster DH et al. Cancer Incidence in Five Continents Vol. 10. International Agency for Research on Cancer Lyon, France 2014.

3. Foucher ES, Colombet M, Reis LA et al. International incidence of childhood cancer, 2001–2010: a population-based registry study. Lancet Oncol.

2017;18(6):719–31. doi: 10.1016/S1470-2045(17)30186-9

4. Spector LG, Pankratz N, Marcotte EL. Nongenetic Genetic and nongenetic risk factors for childhood cancer. Pediatr Clin North Am. 2015; 62(1): 11–25.

5. Stiller CA, ed. Childhood cancer in Britain: incidence, survival, mortality. Oxford, Oxford University Press, 2007.

6. Christensen K, Savage S, Huntington N, et al. Epidemiology and genetics of childhood cancer. Journal of Empirical Research on Human Research Ethics 2017; 12 (2): 97 –106. doi: 10.1177/1556264617697839

7. Belson M, Kingsley B, Holme A. Risk factors for acute leukemia in children: a review. Environmental Health Perspectives, 2007, 115:138-45.

8. O'Connor SM, Boneva RS. Infectious etiologies of childhood leukemia: plausibility and challenges to proof. Environmental Health Perspectives, 2007, 115:146–50.

9. Zachek CM, Miller MD, Christopher H. et al. Children's Cancer and Environmental Exposures: Professional Attitudes and Practices. Journal of Pediatric Hematology/Oncology: 2015; 37(7), 491–7.

10. Urayama KY, Wiencke JK, Buffler PA et al. MDR1 gene variants, indoor insecticide exposure, and the risk of childhood acute lymphoblastic leukemia. Cancer Epidemiology Biomarkers and Prevention, 2007, 16:1172–77.

11. Abbasi S, Maleha F, Shoba K. Acute Lymphoblastic Leukemia Experiences: epidemiology and Outcome of Two Different Regimens. Mediterr J Haematol Infect Dis 2013; 5(1): e2013024.

12. Committee on Medical Aspects of Radiation in the Environment (COMARE). Eleventh report. The distribution of childhood leukaemia and other childhood cancers in Great Britain. London, Health Protection Agency, 2006 http://www.comare.org.uk/press _releases/documents/COMARE11thRe port.pdf.

13. Linabery AM, Ross JA. Trends in childhood cancer incidence in the U.S. (1992-2004). Cancer. 2008; 112:416-32.

14. Swami N, Rama R, Shanta V. Childhood cancers in Chennai, India, 1990-2001: Incidence and survival. Int J Cancer 2008; 122:2607–11.

15. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. Cancer Incidence, Mortality and Prevalence Worldwide. Lyon, France: Globocan; 2018. https://doi.org/10.3322/caac.21492

16. Zhang L, Samad A, Pombo-de-Oliveira MS et al. Characteristics of Childhood Acute Promyelocytic Leukemia. Blood Rev. 2015; 29(2): 101–25.

17. Margolin JF, Steuber CP, Poplack DG. Acute lymphoblastic leukemia. In: Pizzo PA, oplack DG, Eds. Principles and Practice of Pediatric Oncology. Philadelphia: Lippincott Williams & Wilkins. 15th ed. 2006. Pp. 538–90.

18. Wagner A. Sarcoma, An Issue of Hematology/Oncology Clinics of North America. Int J Cancer 2012; 13: E508–17.

19. Al Nasser A, El Solh H, De Vol E. Improved outcome for children with acute lymphoblastic leukemia after risk-adjusted intensive therapy: A single-institution experience. Ann Saudi Med 2008; 28(4): 251-9.

20. Aziz SA, Sharma SK, Sabah I, Jan MA. Prognostic significance of cell surface phenotype in acute lymphoblastic leukemia. South Asian J Cancer 2015; 4(2): 91-4.

21. Wigle D, Turner M, Krewski D. A Systematic Review and Meta-analysis of Childhood Leukemia and Parental Occupational Pesticide Exposure. Environ Health Perspect. 2009; 117(10): 1505–13.

22. Arora B, Kanwar V. Childhood cancers in India: Burden, barriers, and breakthroughs. Int J Cancer. 2009;(46)4: 257-9.

23. Moricke A, Zimmerman M, ReiterA. Prognostic impact of age in children and adolescents with acute lymphoblastic leukemia: Data from the trials ALL-BFM 86,90, and 95. Klin Pediatr. 2010; 217: 310-20.

24. Jalal SD, Al-Allawi NA, Al Doski AA. Immunophynotypic aberrancies in acute lymphoblastic leukemia from 282 Iraqi patients. Int J Lab Hematol 2017; 39(6):625-32.

25. Environment in Iraq. UNEP Progress Report, UN, Geneva, 2003. From: http://postconflict.unep.ch/ publications/Iraq_PR.pdf Accessed: 2010.

26. Rajalekshmy KR, Abitha AR, Anuratha N, Sagar TG. Time trend in frequency of occurrence of major immunophenotypes in paediatric acute lymphoblastic leukemia cases as experienced by Cancer Institute, Chennai, and south India during the period 1989-2009: Indian J. Cancer. 2011; 48: 310-15.

27. Koushik A, King W, McLaughlin W. An Ecologic Study of Childhood Leukemia and Population Mixing in Ontario, Canada. Cancer Causes & Control, 2011(12) 6: 483-90.

28. Adam M, Kuehni C, Spoerri A. Socioeconomic Status and Childhood Leukemia Incidence in Switzerland. Front Oncol. 2015; 5: 139.

29. Higgins CD, dos Santos-Silva I, Stiller CA, Swerdlow AJ. Risk Factors for Acute Leukemia in Children: A Review, Season of birth and diagnosis of children with leukemia. An analysis of over 15,000 UK cases. Br J Cancer. 2007. 115(1):138-45•

30. Silverman L. Acute lymphoblastic leukemia. Oncology of infancy and childhood. 2009; 10:279-317.

31. Abdurrahman K, Al Allawi N, Muhsen A. Pattern of Acute Lymphoblastic Leukemia Among Kurdish Children in Duhok City, Northern Iraq: Qatar med. J. 2011;20(2), 17-20.

32. Moricke A, ReiterA, Zimmermann M. 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; 111:4477-89.

33. Tong H, Wang Q, Lu C, Liu Z, Hu Y. Immunophenotypic, cytogenetics and clinical features of 207 acute lymphoblastic leukemia in China. J Pediatr Hematol Oncol 2015; 33:437-41.

34. Kanerva J. The French-American-British (FAB) classification of leukemia. Prognostic factors in childhood acute lymphoblastic leukemia. 2002; 57:1046-51.