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Research Article

Prognostic significance of CD34 expression and HbF level in childhood acute lymphoblastic leukemia

Amena Hameed Muhsin[1], Subh S. Al-Mudallal[2]

1 Department of labrotaries-Imamain Kadimain Medical City, Iraq.
2 Pathology Department, College of Medicine, Al-Nahrain University, Iraq.

Corresponding:
Amena Hameed Muhsin
Department of labrotaries-Imamain Kadimain Medical City, Iraq.
Email: amenahematopathology@gmail.com

Abstract

Background: Acute lymphoblastic leukemia is a heterogeneous malignancy characterized by variable biological and clinical behavior. Multiple diagnostic modalities, including morphological, immunophenotypic, cytogenetic, biochemical and molecular analyses, are essential for its diagnosis and classification. Both CD34 antigen expression and fetal hemoglobin levels have been linked to prognostic outcomes in pediatric acute lymphoblastic leukemia patients.
Objectives: This study aimed to evaluate the prognostic significance of CD34 and hemoglobin F levels in childhood acute lymphoblastic leukemia patients and to explore their correlation with other hematological and clinical parameters.
Method: A cross-sectional study was performed on 28 pediatric patients (<15 years) with a new diagnosis of ALL at the Oncology Department of the Central Teaching Hospital of Pediatrics from August 2017 to April 2018. Data were obtained from each patient using a questionnaire. Peripheral blood and bone marrow samples were analyzed by morphology, cytochemistry and flow cytometry. Hemoglobin F levels were determined using high-performance liquid chromatography.
Results: CD34 expression was detected exclusively among B-lineage acute lymphoblastic leukemia patients and was detected more frequently in children with favorable clinical and hematological prognostic factors.. No associations were detected between HbF levels and any clinical or hematological prognostic factors.
Conclusion: CD34 expression is a common event in childhood B-ALL and is associated with favorable prognostic factors. HbF levels were not associated with any clinical or hematological prognostic factors.

Keywords
Acute lymphoblastic leukemia, CD34 and HbF

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Introduction

Acute lymphoblastic leukemia (ALL) is a malignant clonal disorder of lymphoid progenitor cells resulting from multistep genetic mutations (1). The disease demonstrates considerable heterogeneity in morphology, immunophenotype, cytogenetics and molecular profiles, necessitating integrated diagnostic evaluation to establish classification and prognosis(2). Leukemic cells from patients with ALL express a variety of surface antigens that are also found on normal lymphocyte precursors at discrete stages of maturation (3). Flow cytometric immunophenotyping of childhood ALL plays an important role in the diagnosis and classification of B and T-cell lineages (4). CD34, a 110 to 115 Kd transmembrane sialoglycoprotein, is expressed by early hematopoietic progenitor cells, endothelial cells, and bone marrow (BM) stromal cells and their precursors (5, 6). Although assessment of the number of cells that express the antigen CD34 provides valuable data for diagnostic and prognostic purposes, the percentage of CD34-positive cells should not be considered a substitution for the blast count from the smears or an estimate from the bone marrow biopsy. CD34 is used in acute leukemia and is used to define leukemic blasts (7-9). Previous studies reported a strong correlation between CD34 positivity and favorable prognostic markers, such as younger age, hyperdiploidy and lower leukocyte count(10). Fetal hemoglobin (HbF) is recognized as an indicator of hematological and nonhematological disorders and may be elevated in patients with malignant disorders. Although HbF itself is not a tumor product, its increased synthesis is triggered by malignant conditions(11). Automated high-performance liquid chromatography (HPLC) is an important primary diagnostic method; it can detect hemoglobin variants and hemoglobin A and F percentages in one procedure (12). Some studies have suggested that elevated HbF levels are linked to adverse prognostic parameters, such as organomegaly, anemia and high leukocyte count, in cases of ALL in pediatric patients (11).

Materials and Methods

This cross-sectional study included 28 children under 15 years of age who were newly diagnosed with ALL and admitted to the Oncology Department of the Central Teaching Hospital of Pediatrics between August 2017 and April 2018. The diagnosis was confirmed by peripheral blood and bone marrow examination, including morphology and cytochemical staining. Flow cytometry was conducted at the flow cytometry
Department in Medical City, Baghdad. Written consent was obtained from the patients' guardians before peripheral blood and bone marrow samples were taken. Data, including the main symptoms and physical signs, especially the presence of mediastinal widening; extramedullary manifestations, which include lymphadenopathy, splenomegaly, hepatomegaly, and CNS involvement; and hematological parameters (from the patient case file), were obtained using a questionnaire. The inclusion criteria for the patients were as follows: were younger than 15 years old, were newly diagnosed, and did not receive any treatment before blood samples were collected.

The exclusion criteria for patients were as follows: who received chemotherapy, who had been treated with steroids for more than one week, who had recently received blood transfusions, and who had hemoglobinopathies. Samples of peripheral blood and bone marrow aspirate were stained with Leishman staining in addition to cytochemical staining (with Sudan Black SBB staining and periodic acid-Schiff (PAS) staining). Lymphoblasts that were subjected to PAS staining were considered to be positive for granular staining and strongly positive for block staining.

Other peripheral blood and bone marrow aspirate samples were sent for flow cytometry analysis from each patient in an ethylene diamine tetraacytic acid (EDTA) tube.Flow cytometry device by BD Biosciences (USA), Model: BD FACSCanto™ II. An automated 8-color flow cytometer system configured with multilaser capability was used, and BD FACSDiva™ software was used for data acquisition and analysis. The monoclonal antibodies used were primarily from BD Biosciences (CD34 Antibody Cloning: 8G12). The cutoff percentage of blasts is equal to or greater than 20 %.

For newly diagnosed ALL patients, one cytoplasmic marker, CD3, and two surface markers, CD34 and CD19, were tested in bone marrow aspirates. The FSC/SSC used for gating on the blast window, CD19 and CD3 were used to differentiate between T-ALL and B-ALL, in which B-ALL is CD19 positive and CD3 negative, T-ALL is CD19 negative and CD3 positive, and CD34 was used to study its expression pattern in blasts.

HPLC: is a process in which a mixture of molecules (for example, normal and variant hemoglobins) with a net positive charge is separated into its components by their adsorption onto a negatively charged stationary phase in a chromatography column. D-10 software is used to reduce the amount of raw data collected from each analysis. Two-level calibration is used for the HbA2/F/A1c values. A sample report and a chromatogram are generated for each sample. Peripheral blood samples in EDTA tubes were sent for HPLC to assess HbF levels. The cutoff value for HbF was 1 %. The risk group was classified in this study according to WBC count and age; the high-risk group was older than 10 years and had a WBC count >50000.

Statistical analyses: SPSS v23 was used. Categorial variables were analyzed using the chi-square test or Fisher's exact test, whereas continuous variables were assessed using the Mann-Whitney U test. Significance was accepted at $P < 0.05$.

Results

CD34 expression in ALL

Among 28 pediatric ALL patients, 75 % presented with B ALL, and 25 % with T ALL. The male-to-female ratio was 1.2:1. The median ages were 6 (5.75) years, 5 (4.5), and 10 (6) years for total, B ALL and T ALL patients, respectively, which was not significant ($P = 0.066$).

Common presenting features in order of frequency were as

follows: fever in 96.4 %, hepatosplenomegaly in 96.4 %, lymphadenopathy in 78.6 %, pallor in 71.4 %, CNS involvement in 46.4 %, bruising in 35.7 %, and mediastinal mass in 21.4 %.

CD34 expression was positive in 66.7 % of patients with B ALL and negative in 33.3 %; CD34 expression was negative in all patients with T ALL. CD34 positivity correlated significantly with age (1–10 years; P=0.035; Table 1) but not with sex or hematological variables. Moreover, positive CD34 expression was less frequent in children with CNS involvement (4 (57.1 %) versus 10 (71.4 %)); however, this difference was statistically insignificant (P = 0.870).

Table 1: Association between CD34 expression and age and sex in patients with B ALL.

Age and sex		CD34 positive	CD34 negative	P
Age (years)	1-9	14 (73.7 %)	5 (26.3 %)	0.035 *
	≥ 10	0 (0.0 %)	2 (100.0 %)	
Sex	Male	8 (72.7 %)	3 (27.3 %)	0.8 *
	Female	6 (60.0 %)	4 (40.0 %)	

*: Fischer exact test; S: significant at P < 0.05; NS: not significant at P > 0.05

Hemoglobin F (HbF) levels in patients with ALL

The difference in HbF levels between patients with B and T ALL (1 (1 %) versus 1.1 (0.8 %)) was not significant, as shown in Table 2. Moreover, HbF levels were not significantly associated with age, sex, risk group, hematological parameters or clinical presentation.

Table 2: HbF levels in B-ALL and T-ALL.

HbF %	Total	B ALL	T ALL	P
High	11 (39.3 %)	8 (38.1 %)	3 (42.9 %)	1.000 *
Normal	17 (60.7 %)	13 (61.9 %)	4 (57.1 %)	
Median (IQR)	1 (0.95)	1 (1)	1.1 (0.8)	0.831 †

†: Mann-Whitney U test; not significant, P > 0.05.

Associations between CD34 expression and HbF levels in patients with ALL:

The HbF level in children who were positive for CD34 was 1.00 (1.15), whereas it was 0.80 (0.70) in children who were negative for CD34; these values were not significant (P = 0.764). Although high HbF expression was more frequent in patients with positive CD34 expression, these findings were not significant (Table 3).

Table 3: CD34 and Hb F association.

HbF	CD34 positive	CD34 negative	P
Normal (n = 13)	7 (50.0 %)	6 (85.7 %)	0.266 *
High (n = 8)	7 (50.0 %)	1 (14.3 %)	
Median (IQR)	1.00 (1.15)	0.80 (0.70)	0.764 †

n: number of cases: †: Mann–Whitney U test; *: Yates correction for continuity.

Associations between CD34 expression and the PAS score in patients with ALL:

Compared with patients with negative PAS, all ALL patients with strong PAS expression had significantly higher CD34 expression (P = 0.018) (42.9 % versus 35.7 %) (Table 4 shows all patients with B and T ALL). However, the association between CD34 expression and the PAS score in B ALL patients was not significant (P > 0.05). An association cannot be performed for T ALL, as all patients with T ALL had negative CD34 expression.

Table 4: Association between CD34 expression and PAS in ALL.

		CD34			*P*
		Total	**Positive**	**Negative**	
PAS	Negative	13 (46.4 %)	5 (35.7 %)	8 (57.1 %)	
	Positive	9 (32.1 %)	3 (21.4 %)	6 (42.9 %)	1.000 *
	Strong positive	6 (21.4 %)	6 (42.9 %)	0 (0.0 %)	0.018 †

*: Yates correction for continuity test; †: Mann-Whitney U test; not significant at P >0.05; significant at P < 0.05

Associations between HbF levels and the PAS score in patients with ALL:
HbF levels were not significantly associated with the PAS score in any patient with ALL or according to ALL subtype (B and T ALL), since P was > 0.05 (Table 5).

Table 5: Association between HbF and PAS in ALL patients.

HbF	PAS			
	Total	**Negative**	**Positive**	**Strong positive**
Normal	17	8	7	2
High	11	5	2	4
Median (IQR)	1.00 (0.95)	1.00 (1.20)	0.80 (0.50)	1.45 (1.08)
*P**		Reference	NS 0.735	0.515 (NS)

*: Mann-Whitney U test; NS: not significant at P > 0.05.

Expression of CD34 in standard and high-risk ALL patients:
In all ALL patients, CD34 expression was significantly lower in the high-risk group than in the standard-risk group (31.3 %) (P = 0.022; 75.0 %), as illustrated in Table 6. The difference in CD34 expression between standard-risk and high-risk B ALL patients was not significant. This association is inapplicable for T ALL patients since all of them were negative for CD34. Standard and high-risk groups were classified according to WBC count and age.

Table 5: Association between HbF and PAS in ALL patients.

CD34	**Total**	**High risk**	**standard risk**	**P ***
Positive	14 (50.0 %)	5 (31.3 %)	9 (75.0 %)	0.022
Negative	14 (50.0 %)	11 (68.7 %)	3 (25.0 %)	

*: Chi-square test; significant P < 0.05.

HbF levels in standard and high-risk ALL patients:
Notably, the difference in HbF levels between the high- and standard-risk groups in all ALL patients was not significant (Table 7), nor was the difference in the HbF level between the high-risk group and the high-risk group (P > 0.05). This association was not observed for T-ALL patients since all T-ALL patients were grouped as high risk. Risk groups were classified according to WBC count and age.

Table 7: HbF levels in the high- and standard-risk ALL groups.

HbF	**Total**	**High risk**	**standard risk**	***P***
Normal	17 (58.7 %)	10 (62.5 %)	7 (58.3 %)	1.000 *
High	11 (39.3 %)	6 (37.5 %)	5 (41.7 %)	
Median (IQR)		1.05 (0.95)	0.95 (1.00)	0.658 †

*: Chi square test with Yate's correction for continuity test; †: Mann-Whitney U test; not significant, P > 0.05.

Discussion:

Subtypes of acute lymphoblastic leukemia; This study included 28 pediatric patients with ALL; 75 % of them had B-ALL, and 25 % had T-ALL. These findings were in agreement with those of other studies in Arabic countries (Jordan and Morocco) as well as Brazil and Indonesia(13-16).

Age and sex; All of the patients in this study had a median age of six years; this was in line with the findings of other studies (17–19); however, other studies (20–23) did not report comparable median age values. Specifically, the median age of patients with the B-ALL subtype is 5 years, and that of patients with T-ALL is 10 years; these results are comparable to those of Bachir et al. (15) but differ from the results of other studies (24, 25).

These findings confirm that T-ALL is associated with poor prognosis since patients approximately 10 years old are included in the high-risk group (26).

Moreover, the patient age ranged from 1.2–14 years, which is comparable to that reported by Kashmoola et al. (27) in Mosul. The results of the current study revealed that ALL was more frequent in males than in females, with a ratio of 1.2:1, which was close to the findings of many studies, including those of Iraqi and non-Iraqi (15, 27, 28).

Presentation in a clinical setting; Fever and HSM are the most common presentations, whereas bruising is the least common. Since coagulopathy is less common in ALL than in acute myeloid leukemia and usually mild and no severe hemorrhage is observed (29), this finding is comparable to that of AlMulla et al. (30), but it is not in line with that of Harpani et al. (31), who demonstrated a different distribution of clinical manifestations. Additionally, the mediastinal mass sign was limited to T-ALL patients.

CD34 expression; Our investigation revealed that CD34 expression was detected in only 14 out of 28 ALL patients and was detected in only the B-ALL subtype; this finding was in agreement with that of Campana D et al. (32) in the USA.

CD34 expression was detected in 66.7 % of B-ALL patients in this study and was detected only in children in the favorable age group between 1 and 10 years; these results were comparable to those of other studies (33, 34). Although the male:female ratio was 1.2:1, there was no discernible correlation between CD34 positivity and sex; these results are in agreement with those of other studies (10, 35). In terms of the relationships between CD34 and hematological parameters, the median WBC count in CD34-positive B-ALL patients was much lower than the median WBC count in CD34-negative patients.

Additionally, the median Hb level was higher in CD34-positive ALL patients and CNS involvement was less frequent in these patients and Hb is less frequent in children with CNS involvement. These results were in agreement with the results of other studies (10, 33, 34). These results may indicate a correlation between positive prognostic indicators and CD34 expression.

With respect to risk stratification, CD34 expression in B-ALL patients was lower in the high-risk group than in the standard-risk group (55.6 % versus 75 %), which was similar to the findings of Supriyadi et al. (2012) (35). All the T-ALL patients were classified as high risk, and all of them were CD34-negative.

Fetal hemoglobin level; In the B-ALL group, children with high HbF levels were younger than children with normal HbF levels were; only 1 patient who was over 10 years of age had high HbF levels. In addition, there was no significant association between high HbF levels and patient sex, and none of the hematological parameters were associated with high HbF levels or CNS involvement. In the T-ALL group, children with high HbF levels were younger than children with normal HbF levels were. High HbF levels were not associated with patient sex, and none of the hematological parameters were associated with high HbF levels or CNS involvement. Unfortunately, no similar studies in our country have compared these results; in addition, the results of this study are not comparable to those of an Indian study performed by Mallick et al. (11), who reported that HbF is high in many hematological malignancies, including 30 pediatric patients with ALL, and reported that high HbF is associated with poor prognosis. This may be due to differences in ethnic and geographical distribution.

Positive staining with periodic acid–Schiff; In the current study, 57.2 % of the B-ALL patients stained positive for PAS; 28.6 % of them showed mixed block and granular positivity, and the remaining 28.6 % showed strong positive staining; all of them had block positivity. These results were in line with those of Lilleyman et al. (36) in 1994, who reported 75 % positivity for PAS staining, and Belurkar et al. (2013) reported 66.66 % positivity for PAS staining (37).

In this study, the number of ALL patients whose CD34 expression was positive was greater among those with PAS-positive B-ALL than among those with PAS-negative ALL. Additionally, all B-ALL patients with strong PAS positivity were CD34 positive. Moreover, none of the T-ALL patients showed strong PAS positivity. This finding was in agreement with that of Gassmann et al. (38).

If we propose that CD34 expression is a good prognostic marker, this former relationship clearly revealed that CD34 was detected mainly in B-ALL with strong PAS staining. Some studies have concluded that strong PAS positivity, particularly block positivity, is a feature of ALL with a good prognosis in terms of genetics and treatment response but not independent of other cell characteristics (39).

Conclusion

CD34 expression is a frequent event in childhood ALL, particularly B-ALL. CD34-positive ALL, in comparison to CD34-negative ALL, was associated with favorable clinical and hematological prognostic factors and was associated with the standard risk group. Although they are not independent of other prognostic criteria, PAS staining results may correlate with prognosis in ALL, but these initial findings require validation in larger patient cohorts and follow-up. In addition, the

evaluation of the coexpression of CD34 with CD10 is recommended because the coexpression of both markers is associated with good prognostic parameters and the evaluation of cytogenetic abnormalities such as hyperploidy in relation to CD34 expression.

Author Declarations

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Conflict of Interest

The author declares that there are no competing interests.

Ethical Approval

This study was approved by the Iraqi Board for Medical Specialization (Approval No. 1051; 3 March 2019). Written informed consent was obtained from the patients' guardians before sample collection and data acquisition.

Consent for Publication

Not applicable.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

A.H.M. conceived the study, collected the data, performed the laboratory investigations, analyzed the data, and prepared the manuscript under the scientific supervision of S.S.A. Both authors reviewed and approved the final manuscript.

References

1. Terwilliger T, Abdul-Hay M. Acute lymphoblastic leukemia: a comprehensive review and 2017 updates. Blood Cancer J. 2017 Apr 7;7(4):e549. Available from: https://www.nature.com/articles/bcj20173 doi: 10.1038/bcj.2017.3.
2. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, et al. The 2016 revision to the World Health Organization classification of acute myeloid leukemia and acute lymphoblastic leukemia. Blood. 2016 May 19;127(20):2391-405. Available from: https://ashpublications.org/blood/article/127/20/2391/35255/The-2016-revision-to-the-World-Health doi: 10.1182/blood-2016-03-643544.
3. Al-Badran IM, Al-Rubaie HA, Al-Assadi TF. Childhood acute lymphoblastic leukemia: Immunophenotypic profile and aberrant expression of CD13, CD33, CD117, CD11b, CD16, and CD64. Iraqi Journal of Hematology. 2022 Jan-Jun;11(1):1-7. Available from: https://faculty.uobasrah.edu.iq/uploads/publications/1654854500.pdf doi: 10.4103/ijh.ijh_36_21.
4. Iwamoto S, Deguchi T, Ohta H, Kiyokawa N, Tsurusawa M, Yamada T, et al. Flow cytometric analysis of de novo acute lymphoblastic leukemia in childhood: report from the Japanese Pediatric Leukemia/Lymphoma Study Group. Int J Hematol. 2011 Aug;94(2):185-92. Available from: https://link.springer.com/article/10.1007/s12185-011-0900-1 doi: 10.1007/s12185-011-0900-1.
5. Radu P, Zurzu M, Paic V, Bratucu M, Garofil D, Tigora A, et al. CD34—Structure, Functions and Relationship with Cancer Stem Cells. Medicina (Kaunas). 2023 May 10;59(5):938. Available from: https://www.mdpi.com/1648-9144/59/5/938 doi: 10.3390/medicina59050938.
6. Pui CH, Rivera GK, Hancock ML, Raimondi SC, Sandlund JT, Mahmoud HH, et al. Clinical significance of CD10 expression in childhood acute lymphoblastic leukemia. Leukemia. 1993 Jan;7(1):35-40. Available from: https://pubmed.ncbi.nlm.nih.gov/8418377/.
7. Ye D, Garcia-Manero G, Kantarjian HM, Xiao L, Vadhan-Raj S, Fernandez MH, et al. Analysis of Aurora kinase A expression in CD34(+) blast cells isolated from patients with myelodysplastic syndromes and acute myeloid leukemia. J Hematop. 2009 Mar;2(1):2-8. Available from: https://link.springer.com/article/10.1007/s12308-008-0019-3 doi: 10.1007/s12308-008-0019-3.
8. Quessada J, Petit A, Saultier P, Strullu M, Fenneteau O, Daudignon A, et al. Diagnostic challenge in a case of ambiguous lineage acute leukemia with PICALM::MLLT10 rearrangement. Pediatr Blood Cancer. 2022 Nov;69(11):e29853. Available from: https://onlinelibrary.wiley.com/doi/10.1002/pbc.29853 doi: 10.1002/pbc.29853.
9. Liang J, Wu D, Liu Y, Ma Q, Xue Y, Zhu M, et al. Clinical and laboratory features of patients with CD34(+) acute promyelocytic leukemia. Chinese Journal of Oncology. 2009 Mar;31(3):196-198. Available from: https://pubmed.ncbi.nlm.nih.gov/19615259/.
10. Cascavilla N, Musto P, D'Arena G, Ladogana S, Melillo L, Carotenuto M. Adult and children acute lymphocytic leukemia: clinicobiological differences based on CD34 antigen expression. Haematologica. 1997 Jan-Feb;82(1):31-37. Available from: https://pubmed.ncbi.nlm.nih.gov/9107079/.
11. Mallick D, Karmakar R, Barui G, Gon S, Chakrabarti S. The Prognostic Significance of HbF in Childhood Haematological Malignancies. Indian J Hematol Blood Transfus. 2015 Mar;31(1):116-20. Available from: https://link.springer.com/article/10.1007/s12288-014-0383-3 doi: 10.1007/s12288-014-0383-3.
12. Bain BJ, Daniel Y, Henthorn J, de la Salle B, National Haemoglobinopathy Reference Laboratory. Significant haemoglobinopathies: A guideline for screening and diagnosis. Br J Haematol. 2023 Jun;201(6):1047-1065. Available from: https://onlinelibrary.wiley.com/doi/10.1111/bjh.18794 doi: 10.1111/bjh.18794.
13. Noronha EP, Marinho HT, Thomaz EBAF, Silva CM, Veras GDS, Brito LMO. Immunophenotypic characterization of acute leukemia at a public oncology reference center in Maranhão, northeastern Brazil. Sao Paulo Med J. 2011 Dec;129(6):392-401. Available from: https://www.scielo.br/j/spmj/a/D6VvS9g8FqN7b8YhLzH8v9b/ doi: 10.1590/S1516-31802011000600005.
14. Supriyadi E, Veerman AJP, Sutaryo, Purwanto I, Cloos J. Myeloid Antigen Expression in Childhood Acute Lymphoblastic Leukemia and Its Relevance for Clinical Outcome in Indonesian ALL-2006 Protocol. Journal of Oncology. 2012 May 24;2012:e135186. Available from: https://www.hindawi.com/journals/jo/2012/135186/ doi: 10.1155/2012/135186.
15. Bachir F, Bennani S, Lahjouji A, El-Shamsi TE, Al-Abassi AA, El-Khorassani M, et al. Characterization of Acute Lymphoblastic

Leukemia Subtypes in Moroccan Children. International Journal of Pediatrics. 2009 Dec 10;2009:e674801. Available from: https://www.hindawi.com/journals/ijpedi/2009/674801/ doi: 10.1155/2009/674801.
16. Abbasi N, Kamal N, Al-Kaisi N, Al-Sweedan S, Al-Sharif M. Immunophenotypic Profile of Acute Leukemia Cases Using Multicolor Flow Cytometry; Three Year Experience at King Hussein Medical Center. JRMS. 2015 Sep;22(3):53-58. Available from: https://jrms.jrms.gov.jo/index.php/jrms/article/view/285 doi: 10.12816/0013175.
17. Al-Mulla NA, Chandra P, Khattab M, Senechal J, Al-Ghazaly J, Al-Jadiry MF, et al. Childhood Acute Lymphoblastic Leukemia in the Middle East and Neighboring Countries: A Prospective Multi-Institutional International Collaborative Study (CALLME1) by the Middle East Childhood Cancer Alliance (MECCA). Pediatr Blood Cancer. 2014 Aug;61(8):1403-10. Available from: https://onlinelibrary.wiley.com/doi/10.1002/pbc.25031 doi: 10.1002/pbc.25031.
18. Kostić G, Đurić Z, Bunjevački G. Bone changes, mineral homeostasis in childhood acute lymphoblastic leukemia. Medicine and Biology. 2004 Dec;11(3):123-126. Available from: http://facta.junis.ni.ac.rs/mab/mab200403/mab200403-04.pdf.
19. Halalsheh H, Abuirmeileh N, Rihani R, Bazzeh F, Zaru L, Madanat F. Outcome of childhood acute lymphoblastic leukemia in Jordan. Pediatric Blood & Cancer. 2011 Sep;57(3):385–391. Available from: https://onlinelibrary.wiley.com/doi/10.1002/pbc.23065 doi: 10.1002/pbc.23065.
20. Hassan MK, Ibrahim JJ, Abbas MS. The adverse effects of chemotherapeutic agents in Iraqi patients with acute lymphocytic leukemia during the induction phase. International Journal of Advanced Biological Research. 2013 Oct;3(4):584-592. Available from: https://www.semanticscholar.org/paper/THE-ADVERSE-EFFECTS-OF-CHEMOTHERAPEUTIC-AGENTS-IN-Hassan-Ibrahim/9fcf6027376c67d7100bba60cb46c59bbfba08b3 doi: 10.5958/0974-360X.2019.00997.1.
21. Al-Mudallal SS, Al-Windy SAA, Al-Faisal AHM. The significance of FLT3-ITD mutation and Nucleophosmin mutation in acute leukemia. Iraqi J Med Sci. 2013 Winter;11(1):70-77. Available from: https://www.iasj.net/iasj/download/9df5c17e49d1ec30.
22. Feller M, Adam M, Zwahlen M, Bouchardy C, Niggli F, Kuehni C, et al. Family Characteristics as Risk Factors for Childhood Acute Lymphoblastic Leukemia: A Population-Based Case Control Study. PLoS One. 2010 Oct 12;5(10):e13156. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0013156 doi: 10.1371/journal.pone.0013156.
23. Li SY, Ye JY, Meng FY, Li CF, Yang M. Clinical characteristics of acute lymphoblastic leukemia in male and female patients: A retrospective analysis of 705 patients. Oncol Lett. 2015 Jul;10(1):453-458. Available from: https://www.spandidos-publications.com/10.3892/ol.2015.3202 doi: 10.3892/ol.2015.3202
24. Campana D, Pui CH. Detection of minimal residual disease in acute leukemia: methodologic advances and clinical significance. Blood. 1995 Mar 15;85(6):1416–34. Available from: https://ashpublications.org/blood/article/85/6/1416/133134/Detection-of-minimal-residual-disease-in-acute.
25. Sidhom I, Shaaban K, Soliman S, El-Din NH, Attia AS. Clinical Significance of Immunophenotypic Markers in Pediatric T-cell Acute Lymphoblastic Leukemia. Journal of the Egyptian Nat Cancer Inst. 2008 Jun;20(2):111-120. Available from: https://pubmed.ncbi.nlm.nih.gov/20029466/.
26. Testi AM, Attarbaschi A, Valsecchi MG, de Lorenzo P, Cario G, Conter V, et al. Outcome of adolescent patients with acute lymphoblastic leukaemia aged 10–14 years as compared with those aged 15–17 years: Long-term results of 1094 patients of the AIEOP-BFM ALL 2000 study. Eur J Cancer. 2019 Dec;122:61-71. Available from: https://www.ejcancer.com/article/S0959-8049(19)30678-7/fulltext doi: 10.1016/j.ejca.2019.09.004.
27. Kashmoola MA, Abdul-Ameer SJ, Gzeer LF. Chromosomal Changes in Childhood Acute Lymphoblastic Leukemia in Mosul. J Med J. 2011 Jun;45(2):190-194. Available from: https://journals.ju.edu.jo/JMJ/article/view/2232 doi: 10.13140/2.1.1326.4001
28. Harpani PT, Parmar BJ, Makwana AM. Clinicopathological Profile of Acute Leukemia in Children. J Nepal Paediatr Soc. 2012 Aug;32(2):95-98. Available from: https://www.nepjol.info/index.php/JNPS/article/view/6038 doi: 10.3126/jnps.v32i2.6038.
29. Hoffbrand AV, Higgs DR, Keeling DM, Mehta AB, editors. Postgraduate Haematology. 7th ed. Chichester: Wiley-Blackwell; 2016. p. 384-387. Available from: https://hematologie.usmf.md/sites/default/files/inline-files/Postgraduate%20Haematology%207th%20edition..pdf.
30. Al-Hashimi MMY, Wang X. Trend of leukemia in Ninawa/Iraq. Clinical and Experimental Medical Sciences. 2013 Jun;1(8):353–362. Available from: https://www.m-hikari.com/cems/cems2013/cems5-8-2013/alhashimiCEMS5-8-2013.pdf doi: 10.12988/cems.2013.13029.
31. Mrózek K, Harper DP, Aplan PD. Cytogenetics and molecular genetics of acute lymphoblastic leukemia. Hematol Oncol Clin North Am. 2009 Oct;23(5):991-1010. Available from: https://www.thehematologyatlas.com/article/S0889-8588(09)00072-4/fulltext doi: 10.1016/j.hoc.2009.07.001.
32. Campana D, Behm FG. Immunophenotyping of leukemia. Journal of Immunological Methods. 2000 Sep 21;243(1-2):59-75. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0022175900002283 doi: 10.1016/S0022-1759(00)00228-3.
33. Basso G, Lanza F, Orfao A, Moretti S, Gastoldi G. Clinical and biological significance of CD34 expression in acute leukemia. J Biol Regul Homeost Agents. 2001 Jan-Mar;15(1):68–78. Available from: https://pubmed.ncbi.nlm.nih.gov/11388747/.
34. Pui CH, Hancock ML, Head DR, Rivera GK, Look AT, Sandlund JT, et al. Clinical significance of CD34 expression in childhood acute lymphoblastic leukemia. Blood. 1993 Aug 1;82(3):889-894. Available from: https://ashpublications.org/blood/article/82/3/889/56499/Clinical-significance-of-CD34-expression-in doi: 10.1182/blood.V82.3.889.889.
35. Supriyadi E, Veerman AJP, Sutaryo, Purwanto I, Cloos J. Detection of CD10, CD34 and their combined expression on Childhood Acute Lymphoblastic Leukemia and the association with clinical outcome in Indonesia. Journal of Cancer Therapeutics and Research. 2012 Oct;1(1):1-10. Available from: https://research.vumc.nl/ws/files/317913/302225.pdf doi: 10.7243/2049-7962-1-19.
36. Lilleyman JS, Britton JA, Anderson LM, Richards SM. Periodic acid Schiff reaction in childhood lymphoblastic leukaemia. J Clin Pathol. 1994 Aug;47(8):689-692. Available from: https://jcp.bmj.com/content/47/8/689 doi: 10.1136/jcp.47.8.689.
37. Belurkar S, Mantravadi H, Manohar C. Correlation of morphologic and cytochemical diagnosis with flowcytometric analysis in acute leukemia. Journal of Cancer Research and Therapeutics. 2013 Jan-Mar;9(1):71-79. Available from: https://journals.lww.com/jcrt/fulltext/2013/09010/correlation_of_morphologic_and_

cytochemical.14.aspx doi: 10.4103/0973-1482.110378.
38. Gassmann W, Löffler H, Thiel E, Ludwig WD, Maschmeyer G, Rühl H, et al. Morphological and cytochemical findings in 150 cases of T-lineage acute lymphoblastic leukemia in adults. British Journal of Haematology. 1997 May;97(2):372-382. Available from: https://onlinelibrary.wiley.com/doi/10.1046/j.1365-2141.1997.d01-2171.x doi: 10.1046/j.1365-2141.1997.d01-2171.x.
39. Lilleyman JS. Acute lymphoblastic leukaemia. Eur J Cancer. 1997 Jan;33(1):85-90. Available from: https://www.ejcancer.com/article/S0959-8049(96)00428-5/abstract doi: 10.1016/S0959-8049(96)00428-5.