Evaluation of Interleukin 6 and Interleukin 10 in Patients with Acute Lymphoblastic Leukaemia

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(Ann Coll Med Mosul 2025; 47 (1):103-109).
Received: 24th Feb. 2025; Accepted: 7th Apr. 2025.

ABSTRACT

Background: Acute lymphoblastic leukemia is marked by the abnormal clonal expansion of early hematopoietic precursor cells in the bone marrow. In Mosul City, acute lymphoblastic leukemia is the most common form of leukemia, underscoring the importance of comprehensive evaluation and treatment.

Objectives: To evaluate the serum levels of interleukin 6 and interleukin 10 in patients newly diagnosed with Acute lymphoblastic leukemia and to assess their correlation with clinical and laboratory parameters.

Method: A case-control study, conducted in Nineveh Province from January to October 2024, included 30 newly diagnosed acute lymphoblastic leukemia patients and 30 healthy controls. Hematological, biochemical tests and serum interleukin 6 and interleukin 10 levels (measured by ELISA), were performed at diagnosis and post-induction chemotherapy.

Result: At diagnosis, the mean levels of hemoglobin and platelets in patients were significantly lower than those in healthy controls. In contrast, serum levels of interleukin 6, interleukin 10, and the percentage of blast cells in both peripheral blood and bone marrow were significantly higher. After induction chemotherapy, acute lymphoblastic leukemia patients exhibited a significant reduction in interleukin 10 and interleukin 6 levels and a reduction in blast percentages, along with increases in hemoglobin and platelet counts. A significant correlation was found between interleukin 6 and interleukin 10 levels and the percentage of blast cells pre-and post-treatment. In acute lymphoblastic leukemia patients with low interleukin 6 and interleukin 10 levels, complete remission was achieved.

Conclusion: Interleukin levels decrease post-induction chemotherapy, with lower levels linked to remission and higher levels to incomplete remission, suggesting their potential role as a biomarker for disease progression and treatment response.

Keywords: Acute Lymphoblastic Leukemia, Chemotherapy, Hematological Parameters, Interleukin 6, Interleukin 10.

تقييم الإنترلوكين ٦ والإنترلوكين ١٠ في مرضى ابيضاض الدم الليمفاوي الحاد

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الخلاصة

الخلفية: يتميز ابيضاض الدم الليمفاوي الحاد بالتوسع غير الطبيعي للخلايا السلفية الهيماتوبونية المكونة للدم في نخاع العظم. في مدينة الموصل، يعد ابيضاض الدم الليمفاوي الحاد الشكل الأكثر شيوعًا لابيضاض الدم، مما يؤكد على أهمية التقييم والعلاج الشاملين.

الأهداف: تقييم مستويات مصل إنترلوكين ٦ وإنترلوكين ١٠ في المرضى الذين تم تشخيصهم حديثاً بابيضاض الدم الليمفاوي الحاد، ودراسة علاقتهما بالمتغيرات السريرية والمخبرية.

الطريقة: تم إجراء دراسة حالة-شاهد في محافظة نينوى خلال الفترة من كانون الثاني إلى تشرين الاول ٢٠٢٤، شملت ٣٠ مريضًا مشخّصًا حديثًا ب ابيضاض الدم الليمفاوي الحاد و٣٠ شخصًا سليمًا كمجموعة ضابطة. تم إجراء الاختبارات الدموية والكيميائية الحيوية، بالإضافة إلى قياس مستويات إنترلوكين ٦ وإنترلوكين ١٠ في مصل الدم باستخدام تقنية ELISA، وذلك عند التشخيص وبعد مرحلة العلاج الكيميائي التحريضي.

النتائج: عند التشخيص، كانت المستويات المتوسطة للهيموغلوبين والصفائح الدموية لدى المرضى أقل بشكل ملحوظ مقارنة بالمجموعة الضابطة، في حين كانت مستويات إنترلوكين ٦ وإنترلوكين ١٠ ونسبة الخلايا الأرومية في الدم المحيطي ونخاع العظم أعلى بشكل كبير. بعد العلاج الكيميائي التحريضي، لوحظ انخفاض ملحوظ في مستويات إنترلوكين ٦ وإنترلوكين ١٠، إضافةً إلى انخفاض نسبة الخلايا الأرومية، وزيادة في قيم الهيموجلوبين وعدد الصفائح الدموية. كما أظهرت النتائج وجود ارتباط كبير بين مستويات إنترلوكين ٦ وإنترلوكين ١٠ ونسبة الخلايا الأرومية قبل العلاج وبعده. وفي المرضى الذين كانت لديهم مستويات منخفضة من إنترلوكين ٦ وإنترلوكين ١٠، تم تحقيق الشفاء التام.

الاستنتاج: تنخفض مستويات الإنترلوكين بعد العلاج الكيميائي التحريضي، حيث ارتبطت المستويات المنخفضة بالشفاء التام، في حين ارتبطت المستويات المرتفعة بعدم تحقيق الشفاء الكامل، مما يشير إلى دورها المحتمل كواسم حيوي لتطور المرض والاستجابة للعلاج.

الكلمات المفتاحية: ابيضاض الدم الليمفاوي الحاد، العلاج الكيميائي، المعايير الدموية، الإنترلوكين ٦، الإنترلوكين ١٠.

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is characterized by the abnormal proliferation of hematopoietic lymphoid precursors resulting in the accumulation of malignant clones in the bone marrow, with release into peripheral blood and extramedullary tissues [1]. The etiology of ALL is unknown, but a number of genetic and environmental factors have been associated with the risk for leukemia [2]. It has been stated that inflammation plays an essential role in cancer initiation and proliferation. The key point is the balance between the pro-inflammatory and anti-inflammatory cytokines [3]

Interleukin-10 (IL-10), a key cytokine in immune regulation, has been shown to play a dual role in the development and progression of ALL [4]

Interleukin-6 (IL-6) has an important role in malignancy and its progression and severity. It is produced by leukemia blast cells and helps maintain cancer stem cells in the macroenvironment [5,6]. Therefore, a thorough evaluation of hematological parameters, along with markers such as IL-6 and IL-10, could play a crucial role in improving future treatment strategies and prognosis for ALL patients [7].

The study aims to assess levels of IL-6 and IL-10 in newly diagnosed acute lymphoblastic leukemia (ALL) patients before and after induction chemotherapy. It seeks to correlate these interleukins with hematological parameters and post-induction remission outcomes.

MATERIALS AND METHODS

Patients

This observational case-control study was approved by the Council of the Iraqi Board of Medical Specialization, the hematology department at Ibn-Sina Teaching Hospital, Al-Hadbaa Teaching Hospital, and the Ministry of Health/Nineveh Health Department (protocol No.2024137).

A written consent form was obtained from all participants before the study was conducted.

The study was performed in Nineveh Province at Al-Hadbaa Teaching Hospital and Ibn-Sina Teaching Hospital from January 2024 to October 2024.

It included 30 newly diagnosed acute lymphoblastic leukemia (ALL) patients, confirmed through complete blood count (CBC), blood films, Bone marrow aspiration, and flow cytometry. Additionally, 30 healthy individuals matched by age and sex served as a control group, CBC and blood films were done for them and they were normal.

Inclusion and Exclusion Criteria

Inclusion criteria included all newly diagnosed ALL patients of any age and gender, while exclusions criteria included Patients previously diagnosed with ALL, those on maintenance therapy, or experiencing relapses, and those with active infections or inflammation due to elevated interleukin (IL) levels.

Clinical Examination and Sample Collection

Data were collected from all participants, including age, residence, drug usage, and chronic inflammatory disease histories.

Each patient underwent a physical examination and received hematological and biochemical tests, Blood samples (4 ml) were collected before and after chemotherapy induction.

CBC was analyzed with an automated Sysmex XN-350 analyzer and bone marrow smears were examined.

Serum IL-6 and IL-10 levels were measured using sandwich ELISA (manufacturer Chromate Awareness Technology Inc, sensitivity for IL-10 1.04ng/ml and IL-6 1.03 ng/l, detection range 405 to 630 nm, country USA, serial no.4300-3834) techniques with specific kits.

Statistical Analysis

Data were analyzed using IBM-SPSS 26 and summarized in Excel 2010. Normality was tested with the Shapiro-Wilk test. Categorical data were reported as frequencies, numerical data as means, and standard deviations. One-way ANOVA and Tukey's post hoc test evaluated multiple groups, and paired t-tests assessed group differences. Pearson correlation coefficients were calculated, with $p \leq 0.05$ considered significant.

RESULTS

The study included thirty patients with ALL, 17 male and 13 female. Thirty age and sex-matched healthy controls were included in this study. The mean age of patients of B-ALL (14.18±13.681), T-ALL (27.25±12.892) years, and the mean age of control was (17.66±14.498) years. According to sex male predominance was noticed representing 56.7% with male to female ratio found to be 1.30:1

Table (1) demonstrated that the mean of hemoglobin (Hb) and platelets in B-ALL, and T-ALL were lower in patients than among control, with statistical significance (p value=0.000). On the other hand, the mean of white blood cells (WBC), and level of IL-6 and IL-10 were significantly higher in patients than those in control (p value=0.000).

Table 1. Hematological parameters, IL6, and IL10 levels in B-ALL, T-ALL patients and control at the time of diagnosis.

pre-induction Parameters	Control Mean ±SD	B- ALL Mean ±SD	T- ALL Mean ±SD	p-value *
Hb (g/dl)	12.54±1.148 A	7.62±1.554 B	7.56±0.663 B	0.000
WBC (x 10^9/L)	7.31±2.716 A	49.13±41.546 B	34.19±27.397 B	0.000
Platelet (x 10^9/L)	276.33±62.965 A	53.13±48.658 B	62.87±58.244 C	0.000
IL6 (pg/ml)	5.37±8.367 A	74.31±74.686 B	41.75±63.986 C	0.000
IL10 (pg/ml)	4.21±4.189 A	86.36±54.089 B	78.25±45.703 B	0.000

*One–way ANOVA with Tucky post hoc test; similar letters mean no significant difference while different letters mean a significant difference

After induction chemotherapy, there were statistically significant differences in the mean of Hb, platelet, IL6, and IL10 levels as illustrated in Table (2).

Table 2. Comparison between hematological parameters, IL6, and IL10 levels in B-ALL and T-ALL patients after induction chemotherapy.

Post-induction Parameters	Control Mean ±SD	B- ALL Mean ±SD	T- ALL Mean ±SD	p-value*
Hb (g/dl)	12.54±1.148 A	10.94±2.412 B	12.16±2.206 AB	0.011
WBC (x 109/L)	7.31±2.716	11.02±8.795	11.00±10.623	0.116
Platelet (x 109/L)	276.33±62.965 A	191.45±102.28 B	203.37±115.382 AB	0.002
IL6 (pg/ml)	5.37±8.367 A	9.45±2.188 B	2.80±3.959 A	0.018
IL10 (pg/ml)	4.21±4.189 A	9.25±5.134 B	1.80±1.730 A	0.033

*One–way ANOVA with Tucky post hoc test; similar letters mean no significant difference while different letters mean a significant difference

According to Table 3, WBC, percentage of blasts in peripheral blood (PB%), percentage of blasts in bone marrow (BM%), IL-6, and IL-10 were significantly higher in the pre-induction phase than in the post-induction phase for both B-ALL and T-ALL ($p = 0.000$). In contrast, both B-ALL and T-ALL patients had significantly lower platelet and Hb levels before induction.

Table 3. The comparison of hematological parameters, IL6, and IL10 levels in B-ALL and T-ALL patients in pre-induction and post-induction.

Parameters	B-ALL			T-ALL		
	Pre-induction Mean ±SD	Post- induction Mean ±SD	p-value*	Pre-induction Mean ±SD	Post- induction Mean ±SD	p-value*
Hb (g/dl)	7.62±1.554	10.94±2.412	0.000	7.56±0.663	12.16±2.206	0.001
WBC (x 109/L)	49.13±41.546	11.02±8.795	0.000	34.19±27.397	11.00±10.623	0.000
Platelet (x 109/L)	53.13±48.658	191.45±102.288	0.000	62.87±58.244	203.37±115.382	0.025
Blast PB%	28.13±25.927	3.95±7.266	0.000	15.12±13.442	3.12±8.838	0.043
Blast BM%	60.04±24.271	13.38±21.715	0.000	69.00±23.065	10.87±26.329	0.002
IL6 (pg/ml)	74.31±74.686	9.45±12.188	0.000	41.75±63.986	2.80±3.959	0.000
IL10 (pg/ml)	86.36±54.089	9.25±15.134	0.000	78.25±45.703	1.80±1.730	0.000

*Paired t-test has been used

Pre-induction, in Table 4 IL-6 displayed a mild positive correlation with PB% (r = 0.381) and BM% (r = 0.379), both of which were statistically significant (p = 0.042 and p = 0.039). There was no significant correlation between IL-6 and WBC, HB, or platelets.

Furthermore, IL-10 exhibited a weak direct correlation with blasts in PB% (r = 0.255) and BM% (r = 0.252), both statistically significant (p = 0.025 and p = 0.027). No significant correlations were detected with the other study parameters.

Table 4. Correlations of IL6 and IL10 with the Hematological parameters in pre-induction.

	IL-6		IL-10	
parameters	r-value	p-value*	r-value	p-value*
Hb (g/dl)	-0.007	0.970	-0.349	0.059
WBC (x 10^9/L)	0.215	0.643	0.025	0.895
Platelet (x 10^9/L)	-0.046	0.811	-0.083	0.664
Blast PB%	0.381	0.042	0.255	0.025
Blast BM%	0.379	0.039	0.252	0.027

* Pearson's correlation test

Post-induction, Table 5 depicts that IL-6 had a moderate inverse correlation with hemoglobin (Hb; r = -0.652, p = 0.002) and significant positive correlations with blast percentages in peripheral blood (PB; r = 0.379, p = 0.033) and bone marrow (BM; r = 0.259, p = 0.041), while its correlations with WBC and platelet counts were not significant. In contrast, IL-10 presented mild positive correlations with blast percentages in PB (r = 0.338, p = 0.026) and BM (r = 0.225, p = 0.017), with no other significant correlations observed.

Table 5. Correlations of IL6 and 10 IL with the Hematological parameters in post-induction.

	IL-6		IL-10	
parameters	r-value	p-value*	r-value	p-value*
Hb (g/dl)	-0.652	0.002	-0.073	0.702
WBC (x 10^9/L)	0.338	0.067	0.079	0.678
Platelet (x 10^9/L)	-0.152	0.421	0.035	0.854
Blast PB%	0.379	0.033	0.338	0.026
Blast BM%	0.259	0.041	0.225	0.017

* Pearson's correlation test

Table (6) shows that the mean IL6 and IL10 in remission were lower than those among relapse. The statistical significance of these differences was established at p=0.013 and p=0.036, respectively.

Table 6. Variation of IL6 and IL10 in ALL patients in remission and relapse.

	Patients		**p-value***
	Remission Mean± SD	**Relapse Mean± SD**	
IL6 (pg/ml)	3.05±2.014	25.83±13.044	0.013
IL10 (pg/ml)	2.44±1.662	31.20±20.216	0.036

*Paired t-test has been used

DISCUSSION

ALL is a prevalent type of malignancy with a peak incidence between (1-4) years in children. Generally, ALL shows a favorable response to treatment. Interleukins have an important role as immune modulators and the promotion of lymphocyte differentiation and in the regulation of cell proliferation. Therefore, this is a privileged position in the occurrence and development of ALL[8.] The study included 30 ALL patients and 30 healthy controls. The average age of B-ALL patients was 14.18±13.68 years, and for T-ALL patients, it was 27.25±12.89 years, while the control group's mean age was 17.66±14.50 years. No significant age difference between the patients and controls was observed (P = 0.087), while in Nizzamani, et al.[9], the mean age of ALL patients was 7.5±3.2 years. This variation could be related to the difference in the age group taken in this study which included both pediatric and adult patients [9].The current study found that 56.7% of the patients were male, while 43.3% were female; these results are closely aligned with the study done by Kashmola et al in Mosul 2010 [10], which reported 62.9% male and 37.1% female patients.

At the time of diagnosis, the mean of WBC was statistically higher than those among the control; a similar finding was found in Korean study [11]. This can be explained by the malignant transformation of pluripotent hematopoietic stem cells that causes leucocytosis and increased blasts.

In this study, the serum level of IL 6 in the pre-induction phase of chemotherapy was statistically significantly higher in B-ALL and T-ALL than those in control. This is comparable with Saxena, D et al.[12] and Abd El Maksoud et al[13].

This is due to various cytokines produced by the leukemic blast cells including IL-6 which maintains the malignant stem cells microenvironment, hence, supports the proliferation of leukemic cells [12].

The serum level of IL 10 was significantly increased in B-ALL and T-ALL patients before induction chemotherapy when compared with control. Radwan et al [14], agreed with these results.

After chemotherapy induction in B-ALL patients, the study revealed a significant increase in mean Hb and platelets compared to the pre-induction phase. This agrees with Jatav et al,[15]. On the other hand, the percentage of blast cells in both BM and PB was statistically lower than those before the induction of chemotherapy. This is in line with Ayyanar P. et al[16]. Regarding T-ALL after chemotherapy, the mean of Hb and platelets were significantly higher than those before chemotherapy. Additionally, the percentage of blasts in PB% and B.M were also statistically lower than those in the pre-induction phase. This is comparable with Hoezler D. et al[17].

On the other hand, the serum level of IL-6 and IL-10 decreased after chemotherapy in both T-ALL and B-ALL. This result is comparable with Yang Y. Et al[1].

This can be explained by that chemotherapy induction acts as an inhibitory factor on blast cells which may result in the correction of hematological parameters, decreasing blast count and the levels of IL-6, and IL-10. It is noteworthy that the high levels of IL6, and IL-10 decreased in response to chemotherapy, which suggests that measuring the level of cytokines may assist in the evaluation of therapeutic measures [13].

During the pre-induction phase, IL-6 correlated positively and directly with blasts in PB and BM. No significant correlations were found with WBC, Hb, or platelets, aligning with results from Sugiyama H et al. [18,19].

IL-10 showed weak direct correlations with blasts in PB% and BM% While no statistically significant correlations were found with remaining study parameters. A study by Madleen A. et al. [20] also reported significant correlations between IL-10 and bone marrow blasts. This might be attributed to the fact that IL-6 and IL-10 are cytokines secreted from the blast cells, so when the blast increases, the interleukin levels are also increased.

During the post-induction phase, a moderate inverse correlation was found between IL-6 levels and Hb. Direct correlations were also observed with blasts in PB% and BM%. No significant correlations were found with WBC or platelets. This aligns with studies by Kushwaha et al. [21], Madleen A. et al. [20], and Wu et al. [2],

This could be interpreted as the impact of chemotherapy in eradicating cancer cells and enhancing bone marrow function, leading to reduced cytokine levels and increased Hb levels.

For IL-10, mild direct correlations with blasts in PB% and in BM% were noted, with no significant correlations with other parameters.

These findings are consistent with Bruserud O. et al. [22,23].

The study found that patients with low IL-6 levels achieved remission, whereas those with high IL-6 levels experienced relapse, with statistically significant results. Similar findings were observed for IL-10, where lower levels correlated with remission, while higher levels were associated with relapse. These results align with previous studies by Noorhan & Zedan[24], as well as research conducted in China, Ayyanar P. et al [16].

CONCLUSION

At diagnosis, acute lymphoblastic leukemia (ALL) patients exhibited significantly higher IL-6 and IL-10 levels than healthy controls. While these levels generally decreased after induction chemotherapy, a positive correlation was found between interleukin (IL-6, IL-10) levels and blast percentage in both PB% and BM%, both before and after treatment. These findings pave the way for new research in tumor immunotherapy. Moreover, the study revealed that lower IL-6 and IL-10 levels correlated with remission, while higher levels were associated with relapse.

Acknowledgment

We thank all the patients who participated in this study and the medical and laboratory staff at Ibn Sina and Al-Hadbaa Teaching Hospitals for their support.

Conflict of Interest

All authors declare no conflict of interest.

Funding Declaration

None

REFERENCES

1. Imai K. Acute lymphoblastic leukemia: pathophysiology and current therapy. Rinsho Ketsueki. 2017;58(5):460–70. doi: 10.11406/rinketsu.58.460
2. Tebbi CK. Etiology of Acute Leukemia: A Review. Cancers. 2021; 8;13(9):2256. doi: 2072-6694/13/9/2256.
3. Saleh A, Al-Jubory M, Mohammed S, Al-Hayali T. Evaluation of Interleukin-6 in Lymphoma. Annals of the College of Medicine Mosul. 2021;42(2):162–8. doi:10.33899/mmed.2020.128731.10574.
4. Jiménez-Morales S, Aranda-Uribe IS, Pérez-Amado CJ, Ramírez-Bello J, Hidalgo-Miranda A. Mechanisms of Immunosuppressive Tumor Evasion: Focus on Acute Lymphoblastic Leukemia. Frontiers in Immunology. Frontiers Media S.A. 2021;12(1). doi: 10.3389/fimmu.2021.737340.
5. Rašková M, Lacina L, Kejík Z, Venhauerová A, Skaličková M, Kolář M, et al. The Role of IL-6 in Cancer Cell Invasiveness and Metastasis—Overview and Therapeutic Opportunities. Cells. MDPI; 2022;11(2). doi: 10.3390/cells11223698.
6. Al-Hasso IKQ. Role of Interleukin-6 in Type 1 Diabetes Mellitus (Review of Articles). Annals of the College of Medicine. 2023; 45(1):92–7. doi: 10.33899/mmed.2023.137090.1175.
7. Malard F, Mohty M. Acute lymphoblastic leukemia. The Lancet. 2020 Apr;395(10230):1146–1162. doi: 10.1016/s0140-6736(19)33018-1
8. Niaz H, Malik HS, Mahmood R, Mehmood A, Zaidi SA, Bilal U. CLINICO-HAEMATOLOGIC PARAMETERS AND ASSESSMENT OF POST-INDUCTION STATUS IN ACUTE LYMPHOBLASTIC LEUKEMIA. Journal of Ayub Medical College Abbottabad. 2022 Jun;34(3):458–462. doi: 10.55519/jamc-03-10448
9. Nizzamani GS, Nizamani ZA, Fahim A, Ujjan IU. ACUTE LYMPHOBLASTIC LEUKEMIA: CHROMOSOMAL ABNORMALITIES IN CHILDHOOD REPORTING AT A TERTIARY CARE HOSPITAL OF SINDH. The Professional Medical Journal. 2016 Mar;23(03):12–316. doi: 10.29309/tpmj/2016.23.03.1480
10. Kashmoola MA, Abdul-Ameer SJ, Gzeer LF. Chromosomal changes in Childhood Acute Lymphoblastic Leukemia in Mosul. Jordan Med J. 2011;45(2):190–4. doi: 10.13140/2.1.1326.4001
11. Kong SG, Seo JH, Jun SE, Lee BK, Lim YT. Childhood acute lymphoblastic leukemia with hyperleukocytosis at presentation. Blood Res. 2014;49(1):29. doi: 10.5045/br.2014.49.1.29
12. Saxena D, Dawson L, Gera R. Study of Serum Cytokines (Interleukin-6 and Tumor Necrosis Factor-Alpha) in Acute Leukemias. Journal of Radiation and Cancer Research. 2022 Apr;13(2):74–80. doi: 10.4103/jrcr.jrcr_48_21
13. Abd N, Maksoud E, Ragab HM, Abd MM, Latif E, Abdalla S. Prognostic impact of elevated serum hyaluronic acid, ferritin and interleukin-6 in patients with acute myeloid leukemia. Journal of American Science. 2010;6(10):423–32.
14. Radwan RE, Darwish A, Elsaid AM, El-kholy WM. Exploring the potential of IL-10 for risk assessment and early intervention in pediatric ALL. BMC Cancer. 2024 Dec 1;24(1). doi: 10.1186/s12885-024-12677-w
15. Jatav J, Jain B, Niranjan AK. CLINICOPATHOLOGICAL STUDY OF ACUTE LYMPHOBLASTIC LEUKEMIA - A MULTIPARAMETER STUDY. Journal of Evidence-Based Medicine and Healthcare. 2015 Nov;2(51):8582–8585. doi: 10.18410/jebmh/2015/1184
16. Ayyanar P, Kar R, Dubashi B, Basu D. Post-chemotherapy Changes in Bone Marrow in Acute Leukemia With Emphasis on Detection of Residual Disease by Immunohistochemistry. Cureus. 2021 Dec; doi: 10.7759/cureus.20175

17.Hoelzer D, Ludwig WD, Thiel E, Gassmann W, Loffler H, Fonatsch C, et al. Improved outcome in adult B-cell acute lymphoblastic leukemia. Blood. 1996 Jan;87(2):495–508. doi: 10.1182/blood.v87.2.495.bloodjournal872495
18.Dai Q, Zhang G, Wang Y, Ye L, Shi R, Peng L, et al. Cytokine network imbalance in children with B-cell acute lymphoblastic leukemia at diagnosis. Cytokine. 2023 Sep;169:156267. doi: 10.1016/j.cyto.2023.156267
19.Sugiyama H, Inoue K, Ogawa H, Yamagami T, Soma T, Miyake S, et al. The Expression of IL-6 and its Related Genes in Acute Leukemia. 2009; 21(1–2), 49–52. doi: 10.3109/10428199609067579
20.MADLEEN A. ABDOU, M.D. ZAAE-HMD;, MAI M. SALAH EL-DIN, M.Sc. TSAMD; Assessment of the Serum Level of Interleukin-6 and Interleukin-10 in Newly Diagnosed Acute Myeloid Leukemia Patients and the Response to Induction Chemotherapy. Med J Cairo Univ. 2018;86(6):1565–72. doi: 10.21608/mjcu.2018.56362
21.Kushwaha R, Kumar A, Aggrawal K, Nigam N, Kumar A. Post chemotherapy blood and bone marrow regenerative changes in childhood acute lymphoblastic leukemia a prospective study. Indian J Pathol Microbiol. 2014;57(1):72. doi: 10.4103/0377-4929.130903
22.Wu C, Wang S, Wang F, Chen Q, Peng S, Zhang Y, et al. Increased frequencies of T helper type 17 cells in the peripheral blood of patients with acute myeloid leukemia. Clin Exp Immunol. 2009 Aug;158(2):199–204. doi: 10.1111/j.1365-2249.2009.04011.x
23.Bruserud Ø, Ulvestad E. Human acute lymphoblastic leukemia (ALL) blasts as accessory cells during T-cell activation: differences between patients in costimulatory capacity affect proliferative responsiveness and cytokine release by activated T cells. Cancer Immunology, Immunotherapy. 2003 Feb;52(4):215–225. doi: 10.1007/s00262-002-0364-5
24.Noorhan A-M, Zedan ZK. Effect of the Serum Level of Interleukin-6 and Interleukin-10 on Chemotherapy in Acute Myeloid Leukemia Iraqi Patients. International Journal of Pharmaceutical and Bio-Medical Science. 2023 Nov;03(11). doi: 10.47191/ijpbms/v3-i11-03