



## Evaluation the Level of Interleukin-6 and Interleukin-10 in Patients with Acute Myeloid Leukemia (Interleukins in Acute Myeloid Leukemia)

Hiba Nitham Aldeen <sup>1</sup>, Muna Abdulbasit Kashmoola <sup>2</sup>

### ABSTRACT:

#### BACKGROUND:

Acute Myeloid Leukemia (AML) is a hematopoietic stem cell disease. IL-6 and IL-10 play critical roles in AML pathogenesis; IL-6 regulates hematopoiesis and leukemic blast formation, and IL-10 inhibits pro-inflammatory responses in leukemic cells.

#### OBJECTIVE:

To evaluate IL-6 and IL-10 levels in AML patients and assess their correlation with clinical and laboratory parameters.

#### PATIENTS AND METHODS:

A case-control study, conducted in Nineveh Province from January to October 2024, included 30 newly diagnosed AML patients and 30 healthy controls. Hematological and biochemical tests, including Complete Blood Count, bone marrow aspirate, flow cytometry, and serum IL-6 and IL-10 levels (measured by ELISA), performed at diagnosis and post-induction chemotherapy and compared to the control group.

#### RESULTS:

The mean age of AML patients was  $37.8 \pm 21.5$  years and controls were  $36.8 \pm 22.1$  years, with male-to-female ratio of 1:1.50. At diagnosis, IL-6 and IL-10 levels were significantly higher in AML patients than controls ( $p=0.000$ ). IL-6 was negatively correlated with hemoglobin ( $p=0.002$ ) and platelets ( $p=0.021$ ) and positively correlated with bone marrow blasts ( $p=0.035$ ). IL-10 levels negatively correlated with hemoglobin ( $p=0.022$ ) and platelets ( $p=0.040$ ). Post-induction, hemoglobin and bone marrow blast percentage significantly improved. IL-6 and IL-10 levels decreased but remained high compared to controls. Post-induction IL-6 and IL-10 did not correlated with hematological parameters. Pre-and post-induction comparisons showed significant increases in hemoglobin and decreases in bone marrow blasts ( $p=0.000$ ). IL-6 and IL-10 levels were lower in remission than in relapsed cases ( $p=0.000$ ).

#### CONCLUSION:

IL-6 and IL-10 levels were significantly higher in AML patients than controls, correlating with hemoglobin, platelets, and bone marrow blasts at diagnosis and post-induction. Both cytokines decreased after induction but remained elevated in relapsed cases, suggesting they could be useful biomarkers for monitoring AML therapy and progression.

**KEYWORDS:** Acute Myeloid Leukemia, Interleukin-6, Interleukin-10

<sup>1</sup> M.B.Ch.B, Nineveh health directorate.

<sup>2</sup> M.B.Ch.B., MSC, F.I.B.H. (Path.), University of Mosul/ College of Medicine/ Department of Pathology.



### INTRODUCTION:

Acute Myeloid Leukemia (AML) is a group of hematopoietic stem cell disorders characterized by the accumulation of myeloblasts in the bone marrow and peripheral blood, leading to impairment of the hematopoietic system and loss of normal function, often resulting in fatal complications <sup>(1)</sup>. Both environmental and genetic factors contribute to its development <sup>(2)</sup>. Pathophysiology involves clonal proliferation of myeloid precursors due to genomic and cytogenetic abnormalities <sup>(3)</sup>. Dysregulated cytokine signaling creates a pro-tumorigenic microenvironment, affecting the proliferation and

survival of leukemic cells, contributing to chronic inflammation and potentially promoting hematological malignancies. Pro-inflammatory cytokines (IL-1 $\beta$ , TNF- $\alpha$ , IL-6) increase AML aggressiveness, while anti-inflammatory cytokines (TGF- $\beta$ , IL-10) impede progression <sup>(4,5)</sup>. IL-6 is a pleiotropic multifunctional cytokine that, besides its important function as an acute phase protein in inflammation <sup>(6)</sup>, plays a key role within the network of cytokines involved in the regulation of hematopoiesis and leukemic blast formation <sup>(7,8)</sup>. In the setting of leukemias, IL-6 appears to have both stimulatory as well as

inhibitory effects on clonogenic blast growth, reflecting the heterogeneous biology of this disease <sup>(9,10)</sup>. Interleukin-10 (IL-10), a major anti-inflammatory cytokine, limits immune responses, potentially allowing leukemia cells to escape immune surveillance <sup>(11)</sup>.

## PATIENTS AND METHODS:

### Study design and setting

This observational case-control study was conducted in Nineveh Province at Al-Hadbaa and Ibn-Sina Teaching Hospitals from January to October 2024. It included 30 newly diagnosed acute myeloid leukemia (AML) patients and 30 healthy controls.

### Participants

Participants were newly diagnosed AML cases consecutively according to the inclusion criteria and the controls selected as healthy subjects with matched age and gender.

### Inclusion and exclusion criteria

Inclusion criteria were newly diagnosed AML patients of any age and gender, while exclusions included previous AML diagnoses, patients on maintenance therapy, relapsed cases, and those with active infections or inflammation.

### Ethical considerations

Ethical approval was obtained from the Ministry of Health / Nineveh Health Department (Order No. 2024171), and verbal consent was provided by all participants.

### Clinical examination and sample collection

Clinical assessments included detailed history, physical examination, and blood sampling. 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 for IL-6 1.03 ng/l, detection range 405 to 630 nm, country USA, serial no.4300-3834) techniques with specific kits.

### Data Analysis

Data were summarized using Excel 2010 and analyzed with IBM-SPSS 26. Normality was tested with the Shapiro-Wilk test, and parametric tests were used. Categorical data were presented as frequencies and proportions, while numerical data were expressed as means  $\pm$  standard deviations. Independent t-tests were used for comparisons.

### RESULTS:

The mean age among cases was  $37.8 \pm 21.5$  years, and among controls were  $36.8 \pm 22.1$  years. Age distribution: 3 patients <10 years, 4 patients 10-18 years, and 23 patients >18 years. For controls: 5, 6, and 19 in these age groups, respectively, as shown in Figure (1).

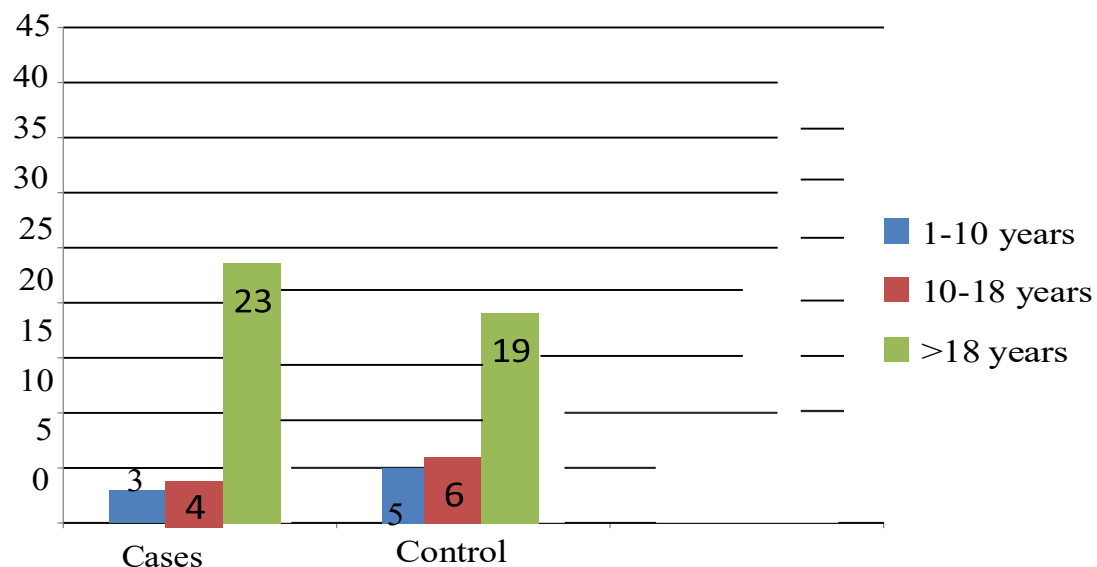


Figure 1: Distribution of the study groups according to age intervals.

## Interleukin-6 and Interleukin-10 in Acute Myeloid Leukemia

The mean hematological parameters were compared between cases and the control group at time of diagnosis (Table 1). Mean hemoglobin (Hb) level and platelet count were significantly

lower in cases compared to controls ( $p=0.000$  for both). Mean WBC level was significantly higher in AML cases and IL6 and IL10 levels were higher in cases than in the control group.

**Table 1: Hematological parameters , IL6 and IL10 variation; in AML cases and control at times of diagnosis.**

Hematological Parameters, IL6&IL10	Cases Mean± SD	Controls Mean± SD	p-value*
Hb (g/dl)	8.3±2.2	12.9±0.7	<b>0.000</b>
WBC (X10 <sup>9</sup> /L)	21.9±30.1	6.7±2.3	<b>0.007</b>
Platelet (X10 <sup>9</sup> /L)	68.6±66.7	255.7±66	<b>0.000</b>
BM. Blasts %	74.2±12.3	-----	-----
P. Bl Blasts %	39.3±13.3	-----	-----
IL6 (pg/ml)	77.2±81.5	3.56±0.59	<b>0.000</b>
IL10 (pg/ml)	123.8±79.7	7.29±4.07	<b>0.000</b>

*\*t-test for independent two means*

Table (2) shows IL6 correlation with hematological parameters at diagnosis. IL6 was significantly and indirectly correlated with hemoglobin ( $r = -0.517$ ;  $p = 0.002$ ) and platelet count ( $r = -0.215$ ;  $p = 0.021$ ) and Significant direct correlation with BM blasts ( $r = 0.442$ ;  $p = 0.035$ ).

No significant correlation with WBC counts or PB blasts. IL10 showed weak but statistically significant indirect correlations with Hb level and platelet count ( $r = -0.396$ ;  $p = 0.022$  and  $r = -0.221$ ;  $p = 0.040$ , respectively).

**Table 2: Correlation of IL6 and IL 10 with hematological parameters at time of diagnosis.**

IL	Parameter	r-value	Asymp.Std. Error <sup>a</sup>	Approx. T <sup>b</sup>	p-value*
<b>IL6</b>	<b>Hb (g/dl)</b>	-0.517	0.211	4.650	<b>0.002<sup>c</sup></b>
	<b>WBC (X 10<sup>9</sup>/L)</b>	0.163	0.265	0.754	0.531 <sup>c</sup>
	<b>Platelet (X 10<sup>9</sup>/L)</b>	-0.215	0.034	-1.823	<b>0.021<sup>c</sup></b>
	<b>Blast in PB%</b>	0.114	0.329	0.218	0.477 <sup>c</sup>
	<b>Blast in BM%</b>	0.442	0.187	3.998	<b>0.035<sup>c</sup></b>
<b>IL10</b>	<b>Hb (g/dl)</b>	- 0.396	0.145	0.691	<b>0.022</b>
	<b>WBC (X 10<sup>9</sup>/L)</b>	0.411	0.254	0.559	<b>0.326<sup>c</sup></b>
	<b>Platelet (X 10<sup>9</sup>/L)</b>	- 0.221	0.170	1.200	<b>0.040<sup>c</sup></b>
	<b>Blast in PB%</b>	0.484	0.236	2.011	<b>0.108<sup>c</sup></b>
	<b>Blast in BM%</b>	0.252	0.231	0.574	<b>0.619<sup>c</sup></b>

a. Not assuming the null hypothesis.

b. Using the asymptotic standard error assuming the null hypothesis.

c. Based on normal approximation.

\* Pearson's correlation test

At the post-induction stage, the hematological differences between cases and the control group showed significant statistical differences for all

parameters (Table 3) also IL6 (56.9±27.5 pg/mL) and IL10 (80.49±70.17 pg/mL) levels in AML cases were significantly higher than in the control group.

Table 3: Hematological parameters, il6 and il 10 variation; AML cases and control post-induction.

Hematological Parameters, IL6 & IL10	Cases Mean± SD	Controls Mean± SD	p-value*
Hb (g/dl)	9.7±2.4	12.9±0.7	0.000
WBC (X10 <sup>9</sup> /L)	17.6±31.7	6.16±2.03	0.044
Platelet (X10 <sup>9</sup> /L)	98.9±108.6	255.7±66.03	0.000
Blast in PB%	38.2±28.5	-----	-----
Blast in BM%	56.8±25.2	-----	-----
IL6 (pg/ml)	56.9±27.5	3.56±0.59	0.000
IL10 (pg/ml)	80.49±70.17	7.29±4.07	0.000

\*t-test for independent two mean

At Post-induction stage, IL6 showed indirect correlations with hemoglobin and platelet count, while weak, direct correlations with WBC, PB blasts, and BM blasts (Table 4). These associations were not statistically significant. IL10 had no significant correlation with hematological parameters.

Table 4: Correlation of IL6 with hematological parameters in post-induction.

IL	hematological parameters	r-value	Asymp.Std . Error <sup>a</sup>	Approx. T <sup>b</sup>	p-value*
IL6	Hb (g/dl)	-0.209	0.116	0.434	0.388 <sup>c</sup>
	WBC (X 10 <sup>9</sup> /L)	0.195	0.259	0.218	0.611 <sup>c</sup>
	Platelet (X 10 <sup>9</sup> /L)	-0.370	0.093	-1.952	0.063 <sup>c</sup>
	Blast in PB%	0.012	0.217	0.061	0.952 <sup>c</sup>
	Blast in BM%	0.250	0.174	1.264	0.218 <sup>c</sup>
IL10	Hb (g/dl)	-0.069	0.165	-0.338	0.738 <sup>c</sup>
	WBC (X 10 <sup>9</sup> /L)	0.024	0.152	0.116	0.909 <sup>c</sup>
	Platelet (X 10 <sup>9</sup> /L)	0.003	0.152	0.016	0.987 <sup>c</sup>
	Blast in PB%	0.114	0.199	0.109	0.707 <sup>c</sup>
	Blast in BM%	0.317	0.234	1.122	0.126 <sup>c</sup>

a. Not assuming the null hypothesis

b. Using the asymptotic standard error assuming the null hypothesis.

c. Based on normal approximation.

\* Pearson's correlation test

Table 5 shows the comparison of hematological parameters in AML cases pre- and post-induction. Hemoglobin level and bone marrow blasts were significantly different between pre- and post-induction. Other parameters showed no

significant differences. IL6 and IL10 levels were higher pre-induction and significantly decreased post-induction (p=0.038 and p=0.018, respectively).

## Interleukin-6 and Interleukin-10 in Acute Myeloid Leukemia

**Table 5: Comparison of hematological parameters , IL6 and IL10 in AML cases pre and post induction.**

Hematological Parameters and IIs	Cases		p-value*
	Pre induction	Post induction	
	Mean± SD	Mean± SD	
Hb (g/dl)	7.9±1.9	9.7±2.4	<b>0.008</b>
WBC (X 10 <sup>9</sup> /L)	24.2±31.8	17.6±31.7	0.471
Platelet (X 10 <sup>9</sup> /L)	66.9±63.6	98.9±108.6	0.223
Blast in PB%	40.1±13.2	38.2±28.5	0.794
Blast in BM%	77.8±13.4	56.5±26.2	<b>0.044</b>
IL6 (pg/ml)	77.2±81.5 (35.50) 8.00; 257.00	56.9±27.5 (28.0) 7.0; 211.0	<b>0.038</b>
IL10 (pg/ml)	123.8±79.7 (87.00) 56.00; 372.00	80.5±70.2 (72.8) 8.0; 365.9	<b>0.018</b>

\*Paired t-test has been used

Table 6 shows IL6 and IL10 variations in AML cases during remission and relapse. Mean IL6 and IL10 levels in remission were significantly lower than in incomplete remission (p=0.000 for both).

**Table 6: Variation of IL6 and IL10 in AML cases in remission and relapse.**

	Cases		p-value*
	Remission	Incomplete remission	
	Mean± SD	Mean± SD	
IL6 (pg/ml)	49.23±25.311	105.15±95.267	<b>0.000</b>
IL10 (pg/ml)	52.11±19.453	111.68±54.878	<b>0.000</b>

\*Paired t-test has been used

## DISCUSSION:

Acute myeloid leukemia (AML) is a malignant hematological disorder marked by the infiltration of bone marrow, blood, and other tissues due to clonal expansion of poorly differentiated hematopoietic cells. It mainly affects bone marrow stem cells, particularly myeloid cells, leading to increased myeloid blasts and impaired blast maturation<sup>(12-14)</sup>. Cytokine signaling abnormalities are key features of leukemia<sup>(15)</sup>.

This study included 30 newly diagnosed AML cases. The mean age in the AML group was 37.8 ± 21.5 years. These figures are comparable to those reported by Alsulami<sup>(16)</sup> (35 ± 22.2 years) and Qassim's study<sup>(17)</sup> (34.67 ± 12.65 years). Regarding gender distribution, 40.0% of AML cases were male and 60.0% female, resulting in a male-to-female ratio of 1:1.5. This is similar to Zawam et al.'s study, which found a male-to-female ratio of 1:1.3<sup>(18)</sup>, while Qassim's study had a ratio of 1.1:1<sup>(17)</sup>. However, the results differ from Tawfiq et al.'s study<sup>(19)</sup>, where 53% of cases were male and 47% female, possibly due to a larger sample size in their study.

Regarding hematological parameters at diagnosis, the current study showed that AML patients had a mean hemoglobin level of 8.3 ± 2.2 g/dL,

consistent with Alwan's study<sup>(20)</sup> and Chang et al.'s study<sup>(21)</sup>. The mean platelet count was 68.6 ± 66.7 × 10<sup>9</sup>/L, lower than the 75 × 10<sup>9</sup>/L reported in Alwan's study<sup>(20)</sup>, the mean white blood cell (WBC) count was 21.9 ± 30.1 × 10<sup>9</sup>/L, significantly higher than Alwan's median of 10 × 10<sup>9</sup>/L, with 10% of patients having counts ≥ 50 × 10<sup>9</sup>/L. These differences may be explained by the clonal proliferation of malignant cells in leukemia, leading to hematopoietic dysfunction, including decreases in other blood cells such as red blood cells, white blood cells, and platelets<sup>(13,14)</sup>.

The study also found that IL-6 and IL-10 levels were significantly higher (p = 0.000) in AML cases compared to the control group. These findings are consistent with studies by Essa<sup>(22)</sup>, Sanchez et al.<sup>(23)</sup> and Alfatlawey et al.<sup>(24)</sup>, all of whom reported significantly increased IL-6 levels in newly diagnosed AML patients. Similarly, Yahya et al.<sup>(25)</sup>, Wu et al.<sup>(26)</sup>, and Alyaqubi et al.<sup>(27)</sup> confirmed that IL-10 levels were significantly higher in AML patients. These results suggest that IL-6 and IL-10 play critical roles in the progression of AML, with cytokines potentially serving as diagnostic indicators for malignancies

(28). IL-6 is involved in both stimulatory and suppressive effects in the setting of leukemias (9,10), while IL-10 displays both immunosuppressive and anti-angiogenic activities, which may promote or inhibit tumor growth (29). Elevated IL-10 levels in AML can both inhibit blast proliferation and promote tumor growth, as IL-10 is versatile in its dual role, acting both as a tumor-promoting factor in some contexts and a tumor-inhibiting factor in others (30,31).

Further analysis showed that IL-6 levels at diagnosis had a statistically significant inverse correlation with hemoglobin (Hb) levels and platelet counts, and a significant positive correlation with the percentage of blast cells in the bone marrow. This was in agreement with Abdel-Hafez et al. (32) and Abd El Maksoud et al. (33), who also observed inverse correlations between IL-6 and Hb, and positive correlations with leukocyte count and blast cells. IL-10, however, was only significantly correlated with Hb and platelet counts, showing indirect correlations with these parameters. This finding contrasts with Wu et al. (26), who found positive correlations between IL-10 and WBC count and blast percentage in bone marrow.

Post-induction, the study revealed that hematological parameters showed significant differences between AML cases and control groups, with hemoglobin and platelet counts being lower in AML patients, while WBC counts were significantly higher. These results align with Abdel-Hafez et al. (32), who also demonstrated variations in hematological parameters before and after induction chemotherapy. IL-6 and IL-10 levels were significantly higher post-induction in AML cases compared to the control group. Mahmood's study (34) similarly supported these findings.

Regarding the correlation between IL-6 and hematological parameters post-induction, this study found an indirect correlation with hemoglobin and platelet counts, and a direct correlation with WBC count, blast percentage in peripheral blood and bone marrow. This finding aligns with Dawood et al. (35). No significant correlations were observed between IL-10 and hematological parameters post-induction, in agreement with Abdel-Hafez et al. (32).

Additionally, significant differences were observed in IL-6 and IL-10 levels between newly diagnosed AML patients and post-induction cases. IL-6 and IL-10 levels significantly decreased after induction chemotherapy ( $p = 0.001$  for IL-6 and  $p = 0.006$  for IL-10). These findings are consistent with Abd El Maksoud et al. (33), who reported that IL-6 levels were higher

in newly diagnosed and relapsed AML patients, with levels decreasing during remission. IL-6's reduction post-induction suggests its potential role in evaluating therapeutic response, as chemotherapy reduces the leukemic burden in AML patients (36). Likewise, IL-10 expression is likely inhibited by chemotherapy, contributing to a decrease in its concentration post-induction.

### CONCLUSION:

IL-6 and IL-10 levels were significantly higher in acute myeloid leukemia (AML) patients compared to healthy controls at diagnosis. IL-6 showed a negative correlation with hemoglobin (Hb) and platelet counts and a positive correlation with bone marrow blast percentage both at diagnosis and post-induction. IL-10 correlated negatively with Hb and platelet counts and positively with bone marrow blast percentage at diagnosis, and negatively with Hb and positively with bone marrow blast percentage post-induction. IL-6 and IL-10 levels were significantly decreased after induction therapy. Furthermore, IL-6 and IL-10 levels were significantly higher in relapsed cases.

### Recommendations

Include conducting future studies with larger sample sizes to confirm the findings, considering IL-6 and IL-10 as potential monitoring biomarkers for therapeutic response and disease progression in AML patients and as prognostic biomarkers to predict relapse and remission, and exploring the correlation between IL-6 and IL-10 levels with molecular and cytogenetic markers in further research

### Authors contribution

**H. A.;** Conceptualization; Investigation; Validation; Visualization; Writing – original draft and Writing – review & editing

**M. A.;** Conceptualization; Investigation; Resources; supervisor; Visualization; Writing – original draft and Writing – review & editing

### Conflict of interest

All authors declare no any conflict of interest.

### Funding declaration

None

### REFERENCES:

1. Fritsche-Polanz R, Fritz M, Huber A, Sotlar K, Sperr WR, Mannhalter C, et al. High frequency of concomitant mastocytosis in patients with acute myeloid leukemia exhibiting the transforming KIT mutation D816V. *Mol. Oncol.* 2010;4(4):335–46. Available at: <https://pubmed.ncbi.nlm.nih.gov/20471335>.
2. Barrett AJ, Le Blanc K. Immunotherapy prospects for acute myeloid leukemia. *Clin.*



- Exp. Immunol.** **2010**; 161: 223–32. Available at: <https://pubmed.ncbi.nlm.nih.gov/20529084>.
3. Vakiti A, Reynolds SB, Mewawalla P, et al. Acute Myeloid Leukemia (Nursing). In: StatPearls. Treasure Island (FL): StatPearls Publishing; **2025**. Available at: <https://pubmed.ncbi.nlm.nih.gov/33760477/> [accessed 20 February 2025].
4. Karimdad Sariani O, Eghbalpour S, Kazemi E, Rafiei Buzhani K, Zaker F. Pathogenic and therapeutic roles of cytokines in acute myeloid leukemia. **Cytokine** **2021**;142: 155508. Available at: <https://pubmed.ncbi.nlm.nih.gov/33810945>.
5. Nagasaki T, Hara M, Nakanishi H, Takahashi H, Sato M, Takeyama H. Interleukin-6 released by colon cancer-associated fibroblasts is critical for tumour angiogenesis: anti-interleukin-6 receptor antibody suppressed angiogenesis and inhibited tumour-stroma interaction. **Br. J. Cancer.** **2014**; 110 (2): 469–478. Available at: <https://pubmed.ncbi.nlm.nih.gov/24346288>.
6. Tanaka T, Narazaki M, Kishimoto T. IL-6 in inflammation, immunity, and disease. **Cold Spring Harb. Perspect. Biol.** **2014**;6(10):a016295. Available at: <https://pubmed.ncbi.nlm.nih.gov/25190079/>
7. Ikebuchi K, Clark SC, Ihle JN, Souza LM, Ogawa M. Interleukin 6 enhancement of multipotential hemopoietic progenitors. **Proc. Natl. Acad. Sci. U.S.A.** **1987**; 84 (24): 9035–39. Available at: <https://doi.org/10.1073/pnas.84.24.9035>.
8. Oster W, Cicco NA, Klein H, Hirano T, Kishimoto T, Lindemann A, et al. Participation of the cytokines interleukin 6, tumor necrosis factor-alpha, and interleukin 1-beta secreted by acute myelogenous leukemia blasts in autocrine and paracrine leukemia growth control. **J. Clin. Invest.** **1989**; 84 (2): 451–57. Available at: <https://pubmed.ncbi.nlm.nih.gov/2788173/>
9. Burger R. Impact of interleukin-6 in hematological malignancies. **Transfus. Med. Hemother.** **2013**; 40 (5): 336–43. Available at: <https://pubmed.ncbi.nlm.nih.gov/24273487>.
10. 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. **Leuk. Lymphoma.** **1996**;21:49–52. Available at: <https://pubmed.ncbi.nlm.nih.gov/7919380>.
11. Wu S, Geßner R, Taube T, Stackelberg Av, Henze G, Seeger K. Expression of interleukin-10 splicing variants is a positive prognostic feature in relapsed childhood acute lymphoblastic leukemia. **J. Clin. Oncol.** **2005**;23:3038–42. Available at: <https://doi.org/10.1200/JCO.2005.00.885>.
12. Tallman MS, Wang ES, Altman JK, Appelbaum FR, Bhatt VR, Bixby D, et al. Acute Myeloid Leukemia, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. **J. Natl. Compr. Canc. Netw.** **2019**; 17 (6): 721–749. Available at: <https://pubmed.ncbi.nlm.nih.gov/28687581>.
13. Allahyari A, Tajeri T, Sadeghi M. Prognostic factors and survival in acute myeloid leukemia cases: A report from the northeast of Iran. **Asian Pac. J. Cancer Prev.** **2016**; 17 (3):1547–51. Available at: <https://pubmed.ncbi.nlm.nih.gov/27039804>.
14. Zahrani M, Al-Quozi A, Alaskar A, Al Faleh A. Clinical features and outcome of acute myeloid leukemia, a single institution experience in Saudi Arabia. **J. Appl. Hematol.** **2015**; 6 (1): 6. Available at: [https://journals.lww.com/jaht/fulltext/2015/06010/clinical\\_features\\_and\\_outcome\\_of\\_a\\_cute\\_myeloid.2.aspx](https://journals.lww.com/jaht/fulltext/2015/06010/clinical_features_and_outcome_of_a_cute_myeloid.2.aspx).
15. Van Etten RA. Aberrant cytokine signaling in leukemia. **Oncogene** **2007**;26:6738–49. Available at: <https://pubmed.ncbi.nlm.nih.gov/17934482>.
16. Alsulami HA, Alnashri MM, Bawazir AF, Alrashid LT, Dly RA, Alharbi YA, et al. Prognostics and clinical outcomes in patients diagnosed with acute myeloid leukemia (AML) in a teaching hospital. **Cureus** **2021**. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8603085/>
17. Al-Rubaie HA, Ahmed E. Effect of remission induction therapy on the level of soluble urokinase plasminogen activator receptor in acute myeloid leukemia. **Iraqi J. Hematol.** **2020**; 9 (2): 87–97. Available at: <https://www.researchgate.net/publication/345745008>
18. Zawam H, Salama RAA, Alsirafy SA, Bishr MK. Treatment outcome of acute myeloid leukemia in Egypt: A developing country perspective. **Int. J. Cancer Treatment** **2019**;1:53–59. Available at: <https://www.researchgate.net/publication/330832597>
19. Tawfiq S, Yassin A, AlGetta H, Hassan K. Acute myeloblastic leukemia: Important clinical and epidemiological facts from

- Hiwa Hospital in Sulaimaniyah, Iraq. **Iraqi J. Hematol.** **2019**; 8 (2): 69–79. Available at: <https://www.researchgate.net/publication/336601761>.
20. Alwan AF, Zedan ZJ, Salman O. Acute myeloid leukemia: Clinical features and follow-up of 115 Iraqi patients admitted to Baghdad Teaching Hospital. **Med. J. Tikrit Univ.** **2005**; 1(111): 1–8. Available at: <https://api.semanticscholar.org/CorpusID:21228300>
21. Chang F, Shamsi T, Waryah AM. Clinical and hematological profile of acute myeloid leukemia (AML) patients of Sindh. **J. Hematol. Thromb. Dis.** **2016**; 4 (2). Available at: <https://www.researchgate.net/publication/302976674>
22. Essa SM, Hadi AHA. Assessment of the levels of interleukin-6, interleukin 10, and leukemia inhibitory factor in patients with acute myeloid leukemia in Dhi Qar Governorate. **Iraqi J. Biotechnol.** **2016**;15(1):61–67. Available at: <https://doi.org/10.36320/ajb/v16.i2.16364>.
23. Sanchez-Correa B, Bergua JM, Campos C, Gayoso I, Arcos MJ, Bañas H, et al. Cytokine profiles in acute myeloid leukemia patients at diagnosis: Survival is inversely correlated with IL-6 and directly correlated with IL-10 levels. **Cytokine** **2013**;61(3):885–91. Available at: <https://pubmed.ncbi.nlm.nih.gov/23357299>.
24. Al-Fatlawey ES, Hussein A, Omara AM. Interleukin-6 level is a powerful predictor of risk for acute myeloid leukemia (AML) among Iraqi patients. **Int. J. Health Sci.** **2022**;11(1):107–16. Available at: <https://media.neliti.com/media/publications/575456-interleukin-6-level-is-a-powerful-predic-2e8560f6.pdf>
25. Yahya DJ, Al-Maaroof ZW, Hassoon AF. Evaluation of leukemia inhibitory factor, interleukin-6 and leptin in acute and chronic myeloid leukemia in Babylon Province. **Med. J. Babylon** **2016**; 13(2):513–21. Available at: <https://api.semanticscholar.org/CorpusID:85524237>.
26. Wu H, Li P, Shao N, Ma J, Ji M, Sun X, et al. Aberrant expression of Treg-associated cytokine IL-35 along with IL-10 and TGF- $\beta$  in acute myeloid leukemia. **Oncol. Lett.** **2012**; 3(5): 1119–23. Available at: <https://pmc.ncbi.nlm.nih.gov/articles/PMC3389635>
27. Alyaqubi KJ, Alkaabi AJ, Alkaabi SJ. Plasma IL-10 concentration and its role in the pathogenesis of acute myeloid leukemia: A prospective study. **Iraqi J. Biotechnol.** **2016**; 15(1): 61–67. Available at: <https://www.researchgate.net/publication/329988715>
28. Binder S, Luciano M, Horejs-Hoeck J. The cytokine network in acute myeloid leukemia (AML): A focus on pro- and anti-inflammatory mediators. **Cytokine Growth Factor Rev.** **2018**;43:8–15. Available at: <https://doi.org/10.1016/j.cytogfr.2018.08.004>
29. Howell WM, Rose-Zerilli MJ. Interleukin-10 polymorphisms, cancer susceptibility and prognosis. **Familial Cancer** **2006**;5(2):143–49. Available at: <https://pubmed.ncbi.nlm.nih.gov/16736283>
30. Mocellin S, Marincola FM, Young HA. Interleukin-10 and the immune response against cancer: A counterpoint. **J. Leukoc. Biol.** **2005**;78(5):1043–51. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16204623>
31. Zamarron BF, Chen W. Dual roles of immune cells and their factors in cancer development and progression. **Int. J. Biol. Sci.** **2011**;7(5):651–58. Available at: <https://pubmed.ncbi.nlm.nih.gov/21647333>.
32. Abd El-Hafez ZA, Abdou MA, Ahmed T, Salah El-Din MM. 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. Available at: [https://mjcu.journals.ekb.eg/article\\_563629ff1edddcee26389bb8ec78f5695aab8.pdf](https://mjcu.journals.ekb.eg/article_563629ff1edddcee26389bb8ec78f5695aab8.pdf)
33. Maksoud NA, Ragab HM, Latif MM, Abdalla SH. Prognostic impact of elevated serum hyaluronic acid, ferritin, and interleukin-6 in patients with acute myeloid leukemia. **J. Am. Sci.** **2010**; 109: 6–10. Available at: <https://www.researchgate.net/publication/228345501>.
34. Mahmood E, Ahmed A. Evaluation of interleukin-35 and interleukin-10 in adult acute myeloid leukemia patients before and after induction chemotherapy. **Iraqi J. Hematol.** **2020**;9(2): 82. Available at: [https://journals.lww.com/ijhm/fulltext/2020/09020/evaluation\\_of\\_interleukin\\_35\\_and\\_interleukin\\_10\\_in.6.aspx](https://journals.lww.com/ijhm/fulltext/2020/09020/evaluation_of_interleukin_35_and_interleukin_10_in.6.aspx)
35. Dawood SD. Assessment of IL-6 serum level in patients with acute myeloid



- leukemia. **Iraqi J. Cancer Med. Genet.** **2018**;4(1).Available at: <https://ijcmg.uomustansiriyah.edu.iq/index.php/ijcmg/article/download/51/33>
36. Murphy T, Zhou J, Daher-Reyes G, Gupta V, McNamara C, Minden M, et al. Delayed hematologic recovery in AML patients after induction chemotherapy is associated with inferior relapse-free survival and persistence of preleukemic mutations. **Blood** **2018**;132 (Supplement 1): 992–92. Available at: <https://doi.org/10.1182/blood-2018-99-115518>.