



Cytokines profiling as prognostic markers in newly diagnosed acute myeloid leukemia

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Abstract:

BACKGROUND: Acute myeloid leukemia (AML) is a common acute leukemia in adult. Recent studies have shown that cytokine systems influence leukemic cell biology and clinical investigations. Among various cytokines, interleukin-6 and interleukin-10 (IL-6 and IL-10) participate an essential function in progression of the disease.

OBJECTIVE: The aim of this study is to quantify of IL-6 and IL-10 levels in AML patients who are newly diagnosed and evaluate lipid profile to assess the relationship between lipid profile level and body mass index (BMI) in myeloid leukemic patients.

MATERIALS AND METHODS: Samples were collected from 45 patients with AML from AL-Yarmouk Teaching Hospital in addition to another 45 healthy individuals were served as a control group during a period from October 2015 to October 2016. Patients ages ranged from 40 to 60 years. IL-6 and IL-10 were measured in all patients before any treatments and compared with control group.

RESULTS: There was an increase in age, white blood cell, and hemoglobin in AML patients as compared to control, but it was not significant. There was a significant increase in neutrophils and lymphocyte count, ($P = 0.001$). Furthermore, there was an increase in BMI, fasting blood sugar, and lipid profile except high-density lipoprotein cholesterol for AML patients as compared to control, but it was not significant. There was a significant increase in serum IL-6 and IL-10 for AML patients compared to controls ($P = 0.001$).

CONCLUSIONS: The present study refers that AML patients were associated with high concentration of IL-6 and IL-10 in comparing to the control group.

Keywords:

Acute myeloid leukemia, interleukin-10, interleukin-6

Introduction

Acute myeloid leukemia (AML) is the major frequent type of acute leukemia in adults. Severe infections, resistance, and relapses are the major reasons of death among patients.^[1]

It is a clonal disease manifested through the fast proliferation of immature myeloid cells in the bone marrow with an impaired differentiation program. Despite all progress in the therapy of AML and elevated rates of complete remission after

induction chemotherapy, many patients will eventually relapse and die from the disease.^[2]

This immunosuppressive status might also be accountable for the permanent recurrence of AML and for the failure of immune treatment;^[3] a specific connection among immune changes, leukemia immune escape, and infections has not been elucidated. Investigating in this line, reveal that T-helper cells be essential factors with Th17 cells being one of the main and not completely implicated division to date.^[4] It has been reported that a potential investigative and

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How to cite this article: Ahmed HS, Tahir NT, Obed FA. Cytokines profiling as prognostic markers in newly diagnosed acute myeloid leukemia. *Iraqi J Hematol* 2017;6:65-8.

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Submission: 10-06-2017

Accepted: 07-07-2017

predictive is using cytokine levels in recently diagnosed AML as well as myelodysplastic syndromes.^[5]

Interleukin-6 (IL-6) is an effective and significant feature for the characteristic enlargement, and the function of T- and B-lymphocytes has great actions on cells of hematopoietic method.^[6] IL-6 level in AML patients is improved for inhibitory and stimulatory consequence on clonogenic blast cell growth.^[7]

IL-6 is a dominant prognostic factor in chronic lymphocytic leukemia, large cell lymphoma, and diver achieve in the development of AML blast cell, in addition to inspiration and maintenance of their progression throughout the IL-6/IL-6 receptor signaling arrangement.^[8]

Interleukin-10 (IL-10) is a homodimer proteins; each of them consists of 178 amino acid,^[9] commonly regarded as an anti-inflammatory, and encoded by the IL10 gene, which is located on chromosome 1 and comprises 5 axons.^[10]

The aspire of this study was to quantify of IL-6 and IL-10 levels in AML patients who are newly diagnosed and evaluate lipid profile to assess the relationship between lipid profile level and body mass index (BMI) in myeloid leukemic patients.

Materials and Methods

The blood sample was collected from 45 patients with new diagnosis of AML from AL-Yarmouk Teaching Hospital, in addition to 45 healthy individuals who were considered as a control group.

The period of this study was from October 2015 to October 2016. The cases were diagnosed clinically by consultant hematologist at AL-Yarmouk Teaching Hospital.

The demographic data include age, gender, BMI as well as clinical manifestations, such as bleeding tendency, pallor, bone pain and constitutional symptoms, weakness, respiratory symptoms, organomegaly, and gingival hypertrophy. Hematological parameters were assessed in ethylenediaminetetraacetic acid tube, including white blood cell (WBC), hemoglobin (Hb), neutrophil, and lymphocyte count, were measured and compared between the two groups.

Fasting blood sugar (FBS) and lipid profile, including total cholesterol (TC), triacylglycerol (TAG), high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol (LDL-C), were determined in both groups using enzymatic colorimetric methods while the concentration of IL-6 and IL-10 were quantitatively

determined by enzyme-linked immunosorbent assay using ready kits manufactured by the R and D system. (Bio-technique brand/Minnesota university company/USA). Finally, the results were estimated.

Statistical analysis

The statistics were performed by SPSS (Statistical Package of Social Science), version 16 (Chicago, SPSS Inc., USA) program. *T*-test was used to approximate variances involving both groups in permanent factors. A *P* < 0.05 was measured to be significantly considerable.

Results

Clinical manifestations of AML on diagnosis are illustrated in Table 1. At diagnosis, most of the patients (31.11%) had fever (*n* = 14). Anorexia was in (22.22%) while bleeding tendency appears in (17.78%) and pallor in (13.33%).

Demographic, hematological, and biochemical parameters were recorded for all AML patients, as in Table 2. There was an increase in age, WBC, and Hb in

Table 1: Clinical manifestations of acute myeloid leukemia patients

Clinical manifestations	n (%)
Fever	14 (31.11)
Anorexia	10 (22.22)
Bleeding tendency	8 (17.78)
Pallor	6 (13.33)
Bone pain	2 (4.44)
Organomegaly	2 (4.44)
Respiratory symptoms	2 (4.44)
Gingival hypertrophy	1 (2.22)
Total	45 (100)

Table 2: Hematological and chemical laboratory data for acute myeloid leukemia and control

Parameters	Means±SD		<i>P</i>
	AML (n=45)	Control (n=45)	
Gender (male/female)	33/12	23/22	-
Age/years	45.0±8.81	44.42±1.03	0.62
WBC (10 ³ /μl)	13.34±5.85	7.50±0.50	0.45
Hb (g/dl)	10.95±2.23	12.50±1.40	0.73
Neutrophils (10 ³ /μl)	38.51±3.42	6.25±2.30	0.001
Lymphocyte count (10 ³ /μl)	2.57±0.47	23.20±4.51	0.001
BMI (kg/m ²)	26.70±2.90	25.20±3.70	0.60
FBS (mmol/l)	4.22±0.55	4.88±0.53	0.20
TC (mmol/l)	5.13±1.50	4.48±1.52	0.31
TAG (mmol/l)	1.99±0.30	0.8±0.27	0.24
HDL-C (mmol/l)	1.36±1.46	1.66±1.41	0.22
LDL-C (mmol/l)	3.38±0.31	2.66±0.34	0.21

SD = Standard deviation, WBC = White blood cell, Hb = Hemoglobin, BMI = Body mass index, FBS = Fasting blood sugar, TC = Total cholesterol, TAG = Triacylglycerol, HDL-C = High-density lipoprotein cholesterol, LDL-C = Low-density lipoprotein cholesterol, AML = Acute myeloid leukemia

AML patients as compared to control, but it was not significant.

There was a significant increase in neutrophils and lymphocyte count ($P = 0.001$). Furthermore, there was an increase in BMI, FBS, TC, TAG, and LDL-C for AML patients as compared to control, but it was not significant. Distribution of AML according to gender is demonstrated in Figure 1.

Cytokines profile for AML and control are demonstrated in Table 3. There was a significant increase in serum IL-6 and IL-10 for AML patients compared to controls, ($P = 0.001$).

Discussion

The hypothesis of coupling the immune system against cancer, including leukemia, has been postulated for very long time, and numerous clinical attempts have been made in this field. Recently, a large evidence from the preclinical and biological view has demonstrated that leukemia cells, including AML, are critically predisposed by the immunological microenvironment, which clearly plays a role in leukemia growth and development.^[11] AML can happen during any period; however, the occurrence rises with age. Its significance has developed with an aging population.^[12]

As regards age, it was noticed that most patients <60 years. Parallel clarifications were prepared by Yahya *et al.* when observed that the mean age of the AML patient group was (44.43 ± 10.75) years.^[13]

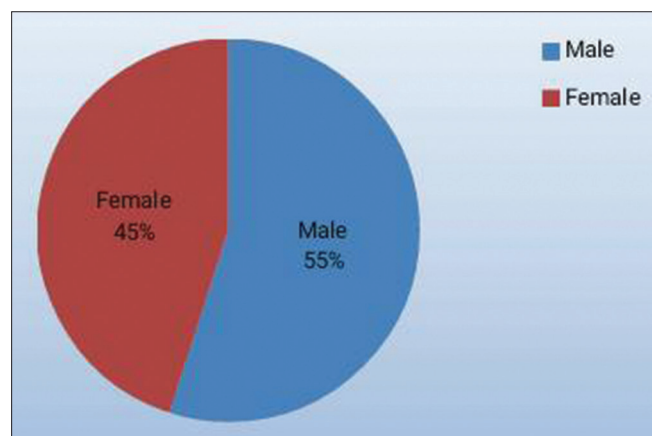


Figure 1: Distribution of acute myeloid leukemia according to gender

Table 3: Cytokines profile for acute myeloid leukemia and control

Parameters ($\mu\text{g/ml}$)	Means \pm SD		P
	AML (n=45)	Control (n=45)	
IL-6	35.30 \pm 1.50	28.60 \pm 1.20	0.001
IL-10	43.58 \pm 1.93	34.51 \pm 1.21	0.001

SD=Standard deviation, AML=Acute myeloid leukemia, IL=Interleukin

In this study, overall male preponderance was found in this study with a percentage of 55% in males (ratio $\approx 1.5:1$). Similar results of gender distribution have been reported in different studies.^[14,15] Main occurrence for all leukemia in males tends to raise as males are comparatively more exposed to work-associated and environmental risks as has been recorded by recent studies.^[16,17]

WBC count is the mainly imperative risk factor for AML complications.^[18] In the present study, WBC count for AML was highest than the control group. This is in agreement with the results of Wetzler *et al.*^[19] This can be demonstrated by the truth that in leukemia there is a clonal proliferation of malignant cells that may arise during any step of maturation in the bone marrow involving myeloid, lymphoid, or pluripotent stages.^[20]

Hb level was 10.95 g/dl in AML patients; this is due to the preponderance of patients were anemic with low Hb levels. There was a significant increase in platelet in AML patients as compared to control group, whereas there was a considerable decreased of neutrophil and lymphocyte in those patients as compared to control group, which is accordance with some studies.^[21,22]

BMI and lipid profile levels in AML patients were not significantly differ from control. This result approved by the study of Rathee *et al.*^[23] This might be interrelated to the high metabolic rate of malignant cells together with the body mass loss that leads to reduce fat substance from cell and so reduce BMI.

Changes in cytokines levels have been associated with autoimmune diseases, allergies, and cancer, involving AML. An inflammatory environment is associated with tumor development and this appears that tumors are dynamic, interacting systems.^[24]

The results in this study explained a higher value of IL-6 and IL-10 for *de novo* AML patients than controls. This result approved by Sanchez-Correa *et al.*^[5]

IL-6 is a pleiotropic cytokine with composite functions in inflammation and metabolic disease. It plays as a proinflammatory cytokine complicated in the acute phase response to tissue injury. It has a causative function in a quantity of inflammatory and autoimmune diseases and its secretion by the adipose tissues participates to metabolic disorder.^[25,26] In addition to its essential function in immune response and inflammatory processes, the function of IL-6 in the angiogenesis, migration, cancer development, and during carcinogenesis is very vital. In many cancer types, IL-6 cannot perform a role in cancer defense; on the contrary, it is concerned in cancer development.^[27]

Musuraca *et al.* noticed that Th17 cells with a double production of IL-10 were closely elevated in AML patients. All exceeding facts maintain the theory that an elevation of IL-10 in AML is a method residential by the disease to generate the immunosuppression status, suggesting that IL-10 could be associated with escape of leukemia cells from immune surveillance.^[28]

Conclusions

The present study refers that AML associated with elevated concentration of IL-6 and IL-10. The improved production of IL-6 and IL-10 in AML patients may stimulate as well as raise the risk of unfavorable prognosis.

The identification of these factors and the clarification of their interaction may ultimately allocate therapeutic intervention in cases of atypical regulation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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