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Use of Cytokines Profiling as a Predictive Indicator for Patients Suffering from Acute Myeloid Leukemia

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Abstract

Background: The progression of acute myeloid leukemia (AML) is mostly associated with interleukin-6 and -10 which are variants of cytokines. Background studies have identified a pattern that associates cytokines systems with the manipulation of cell development and the treatment of AML. **Aim:** The purpose of the current research is to determine whether patients of AML have a higher cytokine, interleukins-6 and -10, as compared to a control group that has not been diagnosed with the disease

Materials and Methods: Data was collected from the Iraq Database of patients and 45 patients were considered the study sample. The age range for the patients was determined to be between 39 and 61 years old. Chemical compounds present in both IL-6 and -10, neutrophils and lymphocyte, indicate a significant count bold sugar, lipid profile and low high-density lipoprotein for the clinical sample.

Results: the clinical manifestations of AML after the diagnosis of new patients. The sample indicated that the clinical group had a 31.11% prevalence of fever with another 22.22% with Anorexia and bleeding tendency and pallor representing 8% and 6% respectively and increasing trend in hematological and biochemical metrics for AML patients, no statistical significance was attached to the age, white blood cells, and hemoglobin when compared to the control sample

Conclusion: The current study has confirmed the results of other previous studies in the association of cytokine concentration with the AML disease. Patients that suffer from AML have a lower count of hemoglobin and a higher count of WBC. Tumor development and inflammatory environment association have an interaction with other blood components which have indicated that higher value of IL-6 and -10 is linked with AML patients while analysis of male preponderance with AML is a factor related to environmental interaction and exposure to AML disease-causing factors such as benzene.

Keywords-Acute myeloid leukemia, Cytokines, bleeding tendency, inflammatory diseases, malignant cells.

INTRODUCTION

The myeloid line of blood cells is vulnerable to the development of cancer. AML is a type of cancer that affects the bone marrow through the rapid growth of abnormal cells' buildup. Patients suffering from AML have a variety of symptoms that can be used for diagnosis of the disease level and effects on the patient [1]. AML is considered untreatable but can be managed through a variety of interventions. However, to identify prognosis of the disease, cytokines are taken into account as biomarkers for the disease [2]. Cytokines are soluble proteins whose function is to regulate and mediate immunity and are included in the pathogenesis of various cancers and other diseases. The solubility of these proteins makes them useful tools for the screening and diagnosis classification among other functions. In the screening of AML, the concentration of the cytokines, IL-6 and IL-10, is considered a factor for the prognostic marker in the disease [3]. This study investigates the connection between the cytokines and the disease progression through the consideration of both clinical and control groups [3]. The cytokine concentrations are compared with the control group to indicate whether or not there is a significant association of the cytokines and the disease stages [6] Since the disease is more prevalent in individuals of 60 years and above, the study incorporates the age group of 40 to 60 where a definite diagnosis of the disease has been made. The goal of the study is to calibrate/measure IL-6 and IL-10 levels for sufferers of AML with an evaluation of lipid profiling where Body Mass Index (BMI) and the lipid profile are matched for the target clinical sample [5].

The development of AML starts with the manifestation and proliferation of myeloid cells with the bone marrow [1]. Studies show that the management of AML accounts for intervention procedures such as induction chemotherapy, complete remission of the disease is not possible, and sufferers relapse and die [16]. The immunosuppressive status of the disease is susceptible to the permanence of the AML and the corresponding failure of the immune system [3]. There is a study gap in the development and progression of medical interventions following the lack of a connection between the changes in the immune system, the escape of leukemia immunity, and the associated infections [3]. The accountability of the IL-6 in the detection and prognosis of AML is linked to the functions of T- and B-lymphocytes (Hart. 2005). The level of IL-6 in sufferers of AML influences inhibitory and stimulatory outcomes on the growth of clonogenic blast cell [6]. Previous studies have classified IL-6 as a dominant prognostic factor in the development and progression of chronic lymphocytic leukemia and affected the blast cell [3]. On the other hand, the IL-10 represents a homodimer protein consisting of amino acid, 178, applied as an anti-inflammatory comprised of IL-10 gene's chromosome 1 and five axons [10].

PATIENTS AND METHODS

Study Sample

From the Iraq Patient Database, the data on blood sample collection was acquired from 45 patients and 45 healthy participants representing the control group [7]. The data from the database is time-based, and therefore the coverage included one-year data set running from September 2016 to September 2017 involving the screening of the patients in a clinical setting through hematologist consultation service and activities.

Variables

Factors considered in this case include variables such as demographic data on age, sex of the participant, and BMI [10]. Bleeding tendency and other factors such as bone pain and pallor are factors of clinical manifestations while gingival hypertrophy and respiratory symptoms are considered constitutional symptoms. Ethylenediaminetetraacetic acid tube method is used for the hematological parameter analysis account for a while blood cells lymphocyte count [8], hemoglobin, and neutrophil assessed and compared across the two groups, clinical and control.

Data Analysis

The use of enzymatic colorimetric method involved the determination of both high-density and low-density lipoprotein cholesterol, fasting blood sugar, triacylglycerol, and total cholesterol. The concentrations of both IL-6 and -10 were determined through the assessment of immunosorbent assay's enzyme-link [9]. The method of analyzing the results implemented the use of T-test in the approximation of the variances for factors assessed in both groups. The significance level for the results was set at 95% confidence level, $P = 0.05$. After analysis of the data, we obtained the following results.

RESULTS

Table 1 above illustrates the clinical manifestations of AML after the diagnosis of new patients. The sample indicated that the clinical group had a 31.11% prevalence of fever with another 22.22% with Anorexia and bleeding tendency and pallor representing 8% and 6% respectively [12]. Bone pain, organomegaly, and respiratory complications were all equally represented at 4.44% with the least representatives having gingival hypertrophy.

Table 1: ALM patients-Clinical manifestations

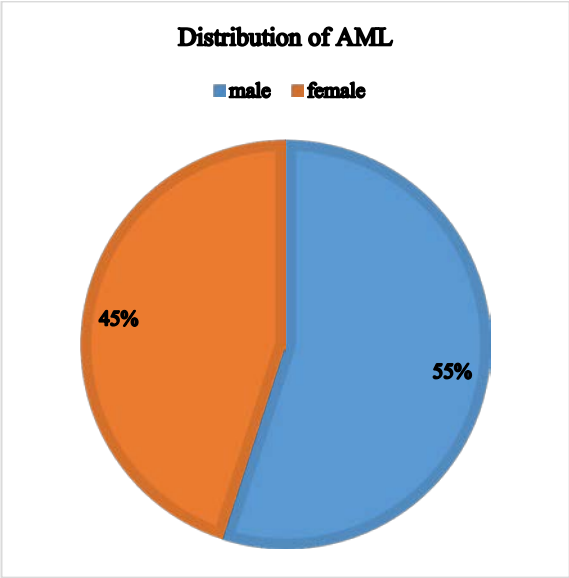
Manifestation- Clinical	n	%
a.Fever	14.00	31.11
b.Anorexia	10.00	22.22
c.Bleeding Tendency	8.00	17.78
d.Pallor	6.00	13.33
e.Bone Pain	2.00	4.44
f.Organomegaly	2.00	4.44
g.Respiratory Symptoms	2.00	4.44
h.Gingival Hypertrophy	1.00	2.22
Total	45.00	100

Although table 2 above shows an increasing trend in hematological and biochemical metrics for AML patients, no statistical significance was attached to the age, white blood cells, and hemoglobin when compared to the control sample [10]. Lymphocyte count ad neutrophils were the only factors that had a statistical significance (P = 0.001) in determining the differences between the control and the clinical samples.

Table 2: Hematological and Chemical Data for AML

Parameters	Mean & SD				P-value
	AML (n = 45)		Control (n = 45)		
Age	45	±	44.42	±1.03	0.62
WBC	13.34	±	7.5	±0.5	0.45
Hb	10.95	±	12.5	±1.4	0.73
Neutrophils	38.51	±	6.25	±2.30	0.001
Lymphocyte	2.57	±	23.20	±4.51	0.001
BMI	26.70	±	23.20	±3.7	0.6

Chart 1: Distribution of AML according to Sex



According to the significance levels in the increase of both lymphocytes and neutrophils and the correlation with factors such as body mass index [BMI], Fasting blood sugar (FBS), total cholesterol [TC], triacylglycerol [TAG], and Low-density lipoprotein cholesterol [LDL-C]. The above chart shows the gender distribution on the above method's factors and shows that males, although the study showed that there were more males than females, the significance levels indicate a higher prevalence of differences among the clinical and control group males [5].

Table 3: AML and Control Group- Cytokines Profile

Parameters	Mean & SD				P-value
	AML (n = 45)		Control (n = 45)		
A.IL-6	35.30	±1.5	28.6	±1.2	0.001
B.IL-10	43.58	±1.93	34.51	±1.21	0.001

The results in Table 3 confirm the increase of "serum IL-6 and -10" for AML sufferers as compared to the control group at a confidence interval of 99%.

DISCUSSION

According to previous studies, the association of age with AML and male preponderance are among factors affecting the distribution and prevalence of the disease. Concerning the ages of the sample populations, a study conducted indicates that the onset and progression of AML were concentrated around 34 to 54 years (44.43 ± 10.75) [15]. On the males' aspect, studies also indicate that males are more likely to develop AML due to the high risks they are exposed at workplaces and their interaction with environmental factors. Exposure to compounds and products with benzene is a variable that shows the differences in the distribution of the disease [6].

White blood cells are associated with the progression of the AML and are considered an imperative risk factor for patients. The findings of the current study indicate that there is a higher level of WBC for the control group [8]. According to a study carried out by Wetzler [16], the same results on the count of WBC were obtained. The association of the results indicates that leukemia is comprised of clonal proliferation involving any phase of maturation of malignant cells within the bone marrow (Alawadi, 2014) [15]. This observation is linked to the involvement of myeloid or lymphoid stages (Larson, n.d).

Hemoglobin levels were observed to be 10.95 grams/deciliter following the fact that majority of patients had low hemoglobin levels. The comparison of patient and control groups concerning platelet in AML shows a significant increase on the former group as compared with the latter. According to studies carried out by Chang, Shamsi, & Waryah (2016) and Kupsa (2016) indicated that a decrease in neutrophil and lymphocyte was an expected outcome for the AML patients unlike with the control group. On the BMI levels as well as the lipid profile indicated that the AML patients differed considerably from the control group. High metabolic rates associated with malignant cells and loss of body mass lead to the reduction of fat from cells resulting in lower BMI as outlined by Rathee [18].

The recorded changes in cytokines levels are effective in influencing autoimmune diseases and cancers that involve AML [16]. Tumor development is also linked to the inflammatory environment leading to interaction with other blood components [15]. The findings of the study indicated that there was a higher value of Il-6 and -10 for the AML patients and the same result was not observed with the control group [13]. IL-6 plays the role of a proinflammatory cytokine since it is the pleiotropic type and offers composite inflammation and metabolic disease functions. As a catalyst to the quantity of autoimmune and inflammatory diseases with the secretion through the participatory function of

the adipose tissues in the development of metabolic disorders [12].

There is a vital association of IL-6 with the functions of inflammatory and autoimmune processes and a variety of other functions in the migration and cancer development as well as during carcinogenesis (Wang, 2014) [15]. While IL-6 can play a defensive role in other clinical manifestations, it does not play the same role as cancer, and instead, it influences the development of cancer and AML progression in this case. Further studies also associate the production of IL-10 with the prevalence of AML. The double production of the IL-10 has been observed to elevate with AML cases unlike it was observed with the control group [19]. Leukemia cells' escape is closely related to the development and progression of AML in that it plays the residential role in generating the immunosuppression status [20,21].

CONCLUSION

The link between AML and the levels of concentration of IL-6 and IL-10 are indicators of the disease prevalence. The current study has confirmed the results of other previous studies in the association of cytokine concentration with the AML disease. Patients that suffer from AML have a lower count of hemoglobin and a higher count of WBC. However, the association of BMI with the disease progression is attached to the metabolic processes and their breakdown of cell fate. Thus, the development of malignant cells is linked to the inflammatory and metabolic diseases' role played by the IL-6 cytokine while the IL-10 is believed to cause Leukemia cell escape. From the comparison of patient and control group factors, the current study concludes that increasing the production of IL-6 and IL-10 is responsible for the stimulation and amplification of risks of undesirable intervention outcomes [20]. Tumor development and inflammatory environment association have an interaction with other blood components which have indicated that higher value of IL-6 and -10 is linked with AML patients while analysis of male preponderance with AML is a factor linked to environmental interaction and exposure to AML disease-causing factors such as benzene.

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