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Original Research Paper

Assessment of the Levels of Interleukin-6, Interleukin-10, and Leukemia Inhibitory Factor in Patients with Acute Myeloid Leukemia in Dhi Qar Governorate

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Abstract: Acute myeloid leukaemia (AML) is a bone marrow-originating form of leukaemia that is capable of metastasizing to multiple organs. The purpose of the study was to investigate the role of serum biomarkers associated with immune responses that fluctuate in Iraqi patients with AML and to assess the changes in these biomarkers. The present study enrolled a total of 100 participants, including 50 males and 50 females, of which 50 had been identified as having AML and the remaining 50 were in good health. Serum levels of leukaemia inhibitory factor (LIF), interleukin-6 (IL-6), and interleukin-10 (IL-10) were estimated in patients with AML. The findings indicated that serum concentrations of IL-6, IL-10, and LIF were significantly elevated ($p<0.05$) in patients with AML relative to healthy individuals. The results provide evidence in favor of the view that the these biomarkers might play a substantial role in the advancement of AML.

Keywords: Biochemical parameters, Immunity response, AML, Iraqi patients.

1. Introduction

Cancer is a clinical condition distinguished by aberrant cellular division and growth; cells circumvent the body's inherent mechanisms that regulate development and acquire the capacity for perpetual multiplication [1].

Leukaemia is a bone marrow-based malignancy. In 2023, the United States documented an estimated 59,610 newly diagnosed instances of leukaemia [2]. The disease was projected to be responsible for 23,710 fatalities. in Iraq, in 2020, leukemia rated fifth (5.34%, 4.22/100,000 P) on the list of malignant diseases affecting both sexes, according to the annual report of the Iraqi Cancer Board [3].

Adults most commonly develop AML, with a specific genetic subtype The disease that affects adults the most frequently is AML, which is classified by a distinct genetic subtype. Acquiring a more comprehensive understanding of the genetic modifications that frequently occur in AML provides significant insights into the fundamental factors that contribute to the aberration in these cells [4].

Cytokines potentially influence multiple aspects of tumour biology, including malignancy initiation, progression, metastasis, angiogenesis, and the emergence of therapy resistance. Moreover, they are correlated with increased disease indications and a diminished life quality among advanced cancer patients [5].

Interleukins, including IL-6 and IL-10, are inflammatory cytokines that have been suggested as possible diagnostic indicators for a range of malignancies [6]. Furthermore, when combined with IL-6 and LIF may exert a substantial influence on the regulation of initial hematopoietic stem cells [7]. Cytokines undeniably have a significant impact on the advancement of hematological malignancies, such as AML [8].

The purpose of this research is to examine a number of biochemical parameters in Iraqis who have been diagnosed with AML in the Dhi Qar Governorate. By measuring IL-6, IL-10, and LIF, it evaluates alterations

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to blood biomarkers and immunity, investigates their function in AML initiation, and considers the possibility that they could be utilized as prognostic factors for identifying the disease.

2.Methodology

Experimental design:

All samples for this investigation were provided by patients who sought treatment and evaluation for AML at the AL-Nasiriyah Teaching Hospital in AL-Nasiriyah City between September 2023 and February 2024.

This investigation involved a sample of Iraqi patients, encompassing both males and females, who had received a confirmed diagnosis of AML through pathology reports. Fifty (50) AML patients as well as fifty (50) healthy individuals were included in this study. Consent was obtained from the participants after they were duly apprised of the study. The scientific committee on ethics gave its approval to the endeavor.

The specimens were procured from asymptomatic subjects who did not present with any preexisting medical conditions or persistent ailments. For this study, the age distribution of the healthy and ill participants was identical.

Estimation of biochemical criteria:

From the cubital vein, a total of five milliliters of venous blood were collected from healthy controls and patients with AML in order to perform the biochemical evaluations. After the serum samples underwent coagulation, they were separated by the centrifugation transferred into Eppendorf containers using a micropipette, and subsequently preserved at -20°C under freezing conditions until analysis [9].

The serum assay kits for human IL-6, IL-10, and LIF quantification were supplied by Solarbio/China. The assays were performed utilizing an enzyme-linked immunosorbent assay (ELISA) in strict adherence to the supplier's instructions.

Statistical analysis:

To determine whether the results derived from this study differed significantly, statistical analyses were conducted using the MedCalc Statistical Software Package (Version 20.215). The independent t-test was employed to make comparisons between numerous groups. The statistical investigation employed measurements of central tendency, particularly the mean, in addition to dispersion, including the standard deviation. For all experiments, a significance level of less than 0.05 was considered appropriate.

3. Results and discussion

The results suggest that there is a statistically significant elevation ($p<0.05$) in the levels of IL-6 and IL-10 in the serum of patients with AML in comparison to the control group of healthy individuals. Figures (1&2). As a result, our results validated the conclusions drawn in previous research [10,11,12].

The study by Abdel-Hafez *et al.* (2018) demonstrated that induction chemotherapy decreased the levels of two prognostic factors (IL-6 and IL-10) in serum of AML patientS. This finding suggests that the quantification of these markers could be utilized to aid in therapy evaluation and prognosis, rendering them highly relevant to routine clinical testing [10].

IL-10, which can be secreted by acute myeloid leukaemia cells, may promote their survival via an autocrine mechanism. In addition, E-cadherin is expressed by AML cells, which may aid in the survival of leukaemia stem cells; IL-10 elevates E-cadherin levels [13].

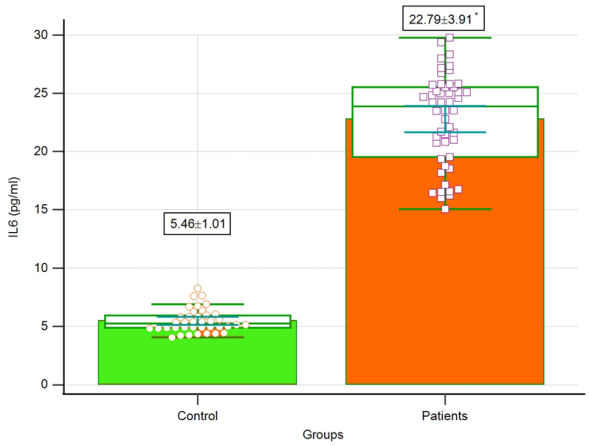

Fig.1. Levels of interleukin-6 in AML patients and the control group.

In multiple recent studies [5,14,15], the functions and marker potential of IL-6 and IL-10 among AML individuals have been examined.

Cytokines, which are categorized according to their pro- or anti-inflammatory functions or cellular origin, are proteins that control homeostasis and immune response by binding to extracellular domains of receptors on the cell surface [16].

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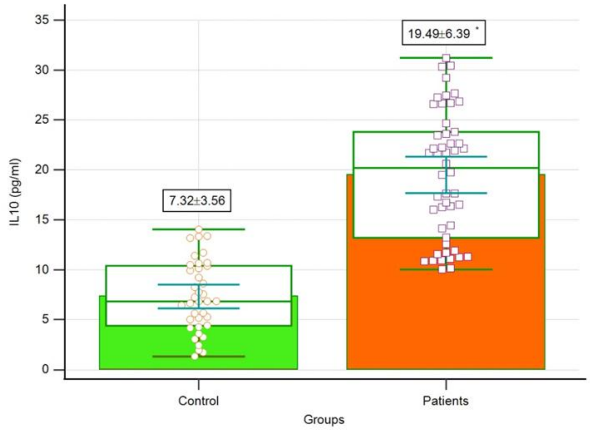

Fig.2. Levels of interleukin-10 in AML patients and the control group.

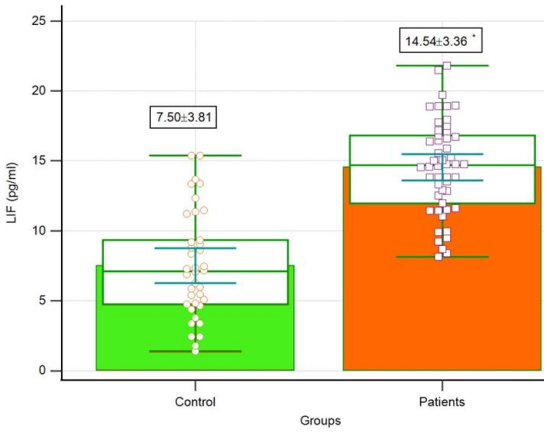

Fig.3. Levels of Leukemia inhibitory factor in AML patients and the control group.

Cytokines are essential mediators in the operation of the immune system. Research has demonstrated that an abnormal discharge of cytokines has a substantial impact on the progression of hematological cancers, AML [5,17].

Interleukins are signaling molecules that play a multifaceted role in numerous diseases and tumors and are involved in the immune system [13].

Interleukins and associated cytokines serve as a means of communication for various cell and tissue types, including adaptive and natural immune system cells. Interleukins play a pivotal role in the development, advancement, and control of cancer [18].

Interleukins promote growth, expansion, and drug resistance while enhancing anti-leukemia immunity and inducing apoptosis [15]. Thus, they play a multifaceted function in AML. IL-6 and IL-10, among other interleukins, are crucial in the development of AML [19].

Interleukin-6 regulates both typical and atypical physiological processes within the organism. The functions governed by these actions are diverse and encompass the development of embryos, wound repair, ageing, inflammation, and immunology, which includes the provision of immunity against COVID-19 [20].

IL-6 levels are significantly increased in the majority of cancer types. Moreover, IL-6 directly promotes the progression of specific diseases, including acute myeloid leukaemia. It appears to operate as a stimulant factor in the development of multiple myeloma, which is produced by stromal cells and malignant cells in the bone marrow [21].

Moreover, according to the findings of Yacoub *et al.* (2020), IL-6 is essential for the progression of AML and may function as a follow-up indicator for the early detection of relapse [22].

Interleukin-10 is an adaptable signaling molecule that plays a vital role in the maintenance of cellular stability and the regulation of inflammation. Its primary function is to regulate the immune response in order to decrease inflammation in the body. IL-10 can, however, function as an immunostimulant under certain conditions [23].

Patients with AML had substantially elevated Th17 cells, that release twice as much IL-10, according to Musuraca *et al.* (2015). The fact that all of these evidence points to the hypothesis that AML induces immunosuppression via elevated IL-10 suggests that IL-10 might be involved in the ability of leukemia cells to evade immune surveillance [24].

Interleukin-10 processes the immune response in a critical manner. IL-10, which is produced by Th2 cells, stimulates the activity of B cells. Macrophage development is inhibited by IL-10 in conjunction with Th1 pro-inflammatory cytokines [8].

In the present investigation, it was observed that AML patients exhibited a substantial rise in serum LIF levels when compared to the comparison group. Figure (3). This finding is consistent with previous research [7]. Conversely, Alizadeh *et al.* (2011) observed that leukemic subjects exhibited reduced concentrations of LIF and IL-6 in their bloodstreams in comparison to their control group [25].

Leukemia inhibitory factor, a constituent of the IL-6 cytokine family, is present in virtually all tissue types of the body. LIF was initially designated by myeloid leukemia cells due to its capacity to stimulate differentiation; however, research on LIF in various solid tumour types and disorders has revealed its potential involvement in numerous other pathologies [26].

Conclusion

The alterations observed in the current investigation establish a noteworthy correlation between heightened levels of IL-6, IL-10, and LIF variables that influence the circulatory system and their involvement in the development and immune reaction of individuals afflicted with AML. To evaluate the utility of interleukins that as a diagnostic markers for the therapeutic response of AML, further research is required.

Ethics

This study was carried out with the endorsement of the clinical ethics council at the University of Kufa in 2017. Parents supplied verbal and written consent, and both subjects and researchers agreed to allow publishing.

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