# Levels of Interleukin-10 in Iraqi Childhood Acute Lymphoblastic Leukemia after Chemotherapy

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## Abstract

**Background:-** Acute Lymphoblastic Leukemia (ALL) is a group of heterogeneous lymphoid disturbance that results from a monoclonal proliferation and expansion of immature T or B lymphocyte ancestor in the blood, bone marrow, and other organs, Interleukin-10 (IL-10) is a pleiotropic cytokine produced by type 2 helper cells (Th2), as well as macrophages and monocytes and neoplastic B lymphocytes and normal.

**Aim of this Study: -** The aim of this study is to estimate the level of IL-10, and its role as an indication of response to chemotherapy treatment.

**Experimental part:-** A probable group study carry on out at Unit of Oncology / Child Center Teaching Hospital / AL-Iskan / Baghdad city during the period from October 2017 to June 2018. 25 patients with newly diagnosis of ALL. IL-10 levels were measured utilize serological methods included the enzyme-linked immunosorbent assay before and after chemotherapy treatment.

**Result**:- This study was carried out on (25) children patients (11 male, and 13 female) newly diagnosed with ALL. The age rang (1.2 years – 12 years), the mean of age was (5.3±3.3 years). A significant decrease in total serum protein and interlukine-10 was observed after chemotherapy ($p<0.001$, 0.001 respectively), and significant increase in GOT, GPT was observed after chemotherapy ($P=0.012$, 1.001 respectively)**.**

**Conclusion: -** The results of our study offering the promising clinical utility of IL-10 as markers of response to chemotherapy.

***Keywords:*** *patients, chemotherapy, lymphoma, acute Lymphoblastic*

## Introduction

Interleukin-10 (IL-10) is a pleiotropic cytokine produced by type 2 helper cells (Th2), as well as macrophages and monocytes, and neoplastic B lymphocytes and normal. It is highly symmetric to an open reading frame of EBV called BCRF1, and EBV infection of B cells up regulates IL-10 production. IL-10 production has powerful immunosuppressive effects by inhibition of Th1 type cytokines, inclusive interferon-gamma and interleukin-2[1]. IL-10 has a strong stimulating effect on B cells, inclusive proliferation, and differentiation. Interestingly, in cell lines derived from B-cell lymphomas, IL-10 has been set up to serve as an anticrime growth factor[2,3]. Serum IL-10 levels have been set up to be substantial forecast factors for Hodgkin lymphoma and when assays that discover both human and viral IL-10 are employed, for NHLs[4] .

Childhood acute leukemia is the generality common cancer in children appears 31% of all cancers and about 3250 new situations per year in the US[5]. Numerous breakthroughs in the past 50 years have increased the survivability of the disease to greatest than 80%, but survivor face long term morbidities[6].

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Acute leukemia is the generality popular cancer in children but the causes of the disease in the plurality of situation are not known. About 80% are the precursor B cell in origin (CD19+, CD10+), and this immunophenotype has increased in happening over the past several contracts in the Western world[7]. ALL is a group of heterogeneous lymphoid defect that results from a monoclonal proliferation and widening of immature B or T lymphocyte progenitor in the blood, bone marrow, and other organs[8]. Proliferation and accumulation of leukemic cells outcome in the repression of normal hematopoiesis and include different particularly the lymph nodes, liver, extramedullary sites, spleen, central nervous system, thymus and gonads[9]. The genetic and epigenetic deviation frequent in the childhood leukemia's are often significant prognostic index and coincidence of several of these are climacteric to modern disease rating protocols[10].

Many studies have shown unprompted IL-10 gene expression and synthesis in a diversity of bone marrow-derived leukemic cells or peripheral blood. These involve B-cells derived from different lymph proliferative disturbance[8]. Since little is known related IL- 10 levels in leukemic before and after chemotherapy treatment, we studied clinical samples of patients with childhood acute Lymphoblastic leukemia (cA LL) for IL-10 levels before and after chemotherapy treatment.

**Experimental part**

**Subjects**

The study was carried out on (25) children patients (11 male, and 13 female) newly diagnosed with ALL. The age rang (1.2 years – 12 years), the mean of age was (5.3±3.3 years), and BMI range was (17.87±7.57 kg/m$^2$).

The selected patients were diagnosed and treated in Unit of Oncology / Child Center Teaching Hospital / AL-Iskan / Baghdad city during the period from October 2017 to June 2018 under the supervision of specialist in pediatric/ oncologist doctors.

**Anthropometric indices measurements**: **Determination of Body Mass Index (BMI)**

Determined the Body mass index by dividing body weight in kilogram by the square of her height in meter. The equation used in medicine produce a unit of measure of kg/m2[11].

**Laboratory methods**

Assay of Total Serum Protein (Biuret method)

Modified Biuret method was used to determine total serum protein using bovine serum albumin as standard[12].

**Determination of Some Enzyme Markers:**

Determination of Alkaline Phosphatase (ALP Activity), GOT, and GPT by using (Kit leaner).

**Determination of serum interlikin-10:-** measurement of IL-10 by used ELISA kit (IBL company, Germany.

## Results

The mean age as (5.3±3.3 years), 54% of them were less than 5 years of age, as shown in Table (1):-

**Table (1): Demographic characteristics of leukemic children**

| Variable | No. | % |
|---|---|---|
| Age mean± SD (5.3±3.3 years) | | |
| <5 years | 13 | 54.16 |
| ≥5 years | 11 | 45.84 |
| Total | 24 | 100.0 |
| Gender | | |
| Male | 10 | 41.66 |
| Female | 14 | 58.34 |
| Total | 24 | 100.0 |

1- Family history and clinical complications:

Only 5 (20.8%) leukemic children had positive family history of leukemia. The associated clinical problems were distributed as followings: 40% of patients have no associated problems, 28% have fever, 16% have headache, 12% have fever & headache and 4% have anemia, as shown in Figures (1, 2).

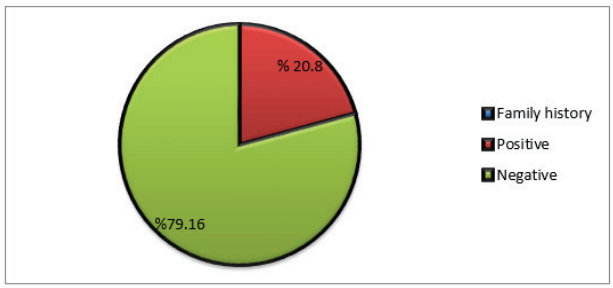


**Figure (1): Distribution of family history.**

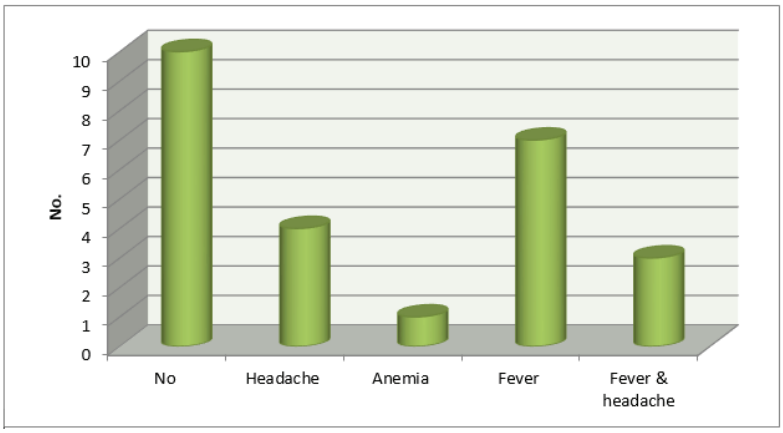


**Figure (2): Distribution of associated clinical problems.**

2- Anthropometric indexes:

The weight of leukemic children was significantly decreased after chemotherapy (p<0.001). There was a highly significant decrease in BMI of leukemic children after chemotherapy (p<0.001)(Table 2):-

**Table (2): Mean ± (SD) levels of anthropometric indexes of leukemic children before and after chemotherapy.**

| Variable | Before chemotherapy | After chemotherapy | P-value |
|---|---|---|---|
| Weight (Kg) | 18.5±8.6 | 16.7±8.2 | <0.001 |
| Waist circum.(Cm) | 58±13.8 | 56.2±15.1 | 0.20 |
| Hip circum.(Cm) | 57.3±15.2 | 59.2±13.1 | 0.50 |
| BMI (Kg/m2) | 14.5±2.2 | 13±2.3 | <0.001 |
| WHR | 1.03±0.17 | 0.96±0.15 | 0.30 |
| WHtR ratio | 0.54±0.13 | 0.56±0.22 | 0.40 |

P value less than< 0.05 is significant

3- Total serum protein, liver functions and Cytokine interlukine-10:

A significant decrease in total serum protein and interlukine-10 was observed after chemotherapy (p<0.001, 0.001 respectively), and significant increase in GOT, GPT was observed after chemotherapy (P=0.012, 1.001 respectively) (Table 3):-

**Table (3): Mean ± (SD) levels of total serum protein, Cytokine interlukine-10, GOT, GPT before and after chemotherapy:-**

| Variable | Before chemotherapy | After chemotherapy | P-value |
|---|---|---|---|
| Total serum protein(g/l) | 48.77+7.8 | 31.21+5.9 | <0.001 |
| ALK | 172.66+82.9 | 196.5+46.2 | 0.147 |
| GOT | 32.58+21.76 | 54.58+29.7 | 0.012 |
| GPT | 19.04+12.7 | 52.04+32.91 | 0.001 |
| Interlukine-10 (Pg/ML) | 66.92+25.09 | 44.57+29.27 | 0.001 |

**P value less than< 0.05 is significant**

## Discussion

### 1: Anthropometric indexes

The current study showed that weight and BMI of leukemic children was significantly decreased after chemotherapy (p<0.001)(table2). This is comparable to results of previous American study which announced that median 6% weight loss after chemotherapy treatment is reveal among leukemic children[13]. Our finding is maladjusted with results of Atkinson et.al, study which present that weight and BMI of leukemic children increased after chemotherapy[14]. Other studies have expounded that children after ALL chemotherapy treatment have a slope to be overweight. However, the generality of the authors confirms the requirement for many surveillance for the developmental disorder of childhood after ALL chemotherapy[15]. Another study acutest out that also a short-term time of monitoring does not permit for a whole estimate of the danger of obesity-related disturbance in children after chemotherapy treatment[16]

### 2: Total serum protein

Serum total protein is a biochemical examination for measured the quantity of total protein in serum. It's using for treatment and diagnosis of types for diseases including the liver, kidney, or bone marrow, as well as other nutritional or metabolic disorders[17].

Our study showed significantly lower levels of total serum protein in leukemic children after chemotherapy (p<0.001) (table 3). This finding is compatible with results by Oleiwi et.al, study who found that total serum protein of leukemic children was significantly reduced at baseline after chemotherapy in comparison to healthy controls[18]. Toxic injury in the liver may be proliferating in practice any known style of injury, including necrosis, cholestasis, steatosis, vascular injury, and fibrosis. During chemotherapy, liver injury may do not be inverted hepatotoxic anticancer agent; the physician should also look response to Antiemetic's, analgesics, antibiotics, or other medications. Pre-existing medicinal problems, tumor, hepatitis viruses, immunosuppression, and other infections, and total parenteral nutrition or nutritional deficiencies; all may be affect a host's ability to liver injury. Therefore In cancer chemotherapy, the liver injury to a toxic reaction is difficult; however, resolution of dosing is oftentimes made instituted on limit toxicity. So basically hepatotoxicity is of major concern and increase non-hepatic toxicity probably caused by altering hepatic rescue. And so on, systematic information for the hepatotoxic effects of chemotherapy is light, and the technique of injury is decided for a few factors[19].

In several types of ALL, total serum protein showed within L1 group patients, no significant differences in the mean levels of total serum protein after 1st and 2nd months of treatment when compared with baseline level, also, within L2 group patients, no significant differences in the mean levels for total serum protein after 1st, 2nd, and 3rd months of treatment when compared with baseline level[18].While, a study showed that significant reduction in total serum protein is due to the effect of disease and low intake of protein[20]. However, some studies inconsistent with the current study which showed that the level of total serum protein not affected or there were a slight decrease in its level due to the effect of corticosteroid which cause increase food intake and metabolism alteration[21, 22]. Other study show decrease in serum total protein concentrations was observed during the ALL induction therapy[23].

**3: levels of interlukine-10:**

This study has seen that serum levels of IL-10 changed during chemotherapy treatment and are capable to be inverted well the path of disease. Serum IL-10 ratios were found higher in active stages of cancer (at diagnosis), while the opposite results with decreased IL-10 was seen after chemotherapy treatment (P=0.001) (Table3). These findings indicate that sequent determinations of serum IL-10 in children with acute lymphoblastic leukemia could support to estimate more exactly the stage of disease and response to therapy in personal patients. As far as we know, this study is the only study to compare the levels of IL-10 before and after chemotherapy in Iraqi children with acute lymphoblastic leukemia

other study showed level of serum IL-10 has been found to essential prognosis factor in some hematologic malignancies[24]. That elevated in the level of IL-10 may be because its resulting by various cells or by malignant cells of the immune system, inclusive monocytes, B and T lymphocytes, and , macrophages[25] .

The reasons and the kind of noteworthy variation in serum IL-10 concentration shown between the stage of cancer growth active and the stage of cancer stillness are complicated. The elevated of serum IL-10 before the inception of treatment and in patients who recrudesce able reflect tumor volume, and illness advancement. Other study in previously the IL-10 is releasing by the cells of many cancer kind[26,27]. On the other hand the surgical excision of the gastrointestinal cancers and colorectal resulted in a significant decreasing of serum IL-10[28]. On the other hand yet a powerful body of guide that IL-10 sport an important Immune-suppressive role[29], letting malignant cells to shun immune monitoring[30] ., and enhance cancer growth and diffusion[26].

## Conclusion

In this study we noted significant decrease in levels of IL-10 after chemotherapy treatment compare with before chemotherapy, this will be clinical advantage for IL-10 as indication of response to chemotherapy treatment. However, it must be confirm that the patients were not sampled at random. The sample collection was chosen very accurately. We recommend that you study the increase of study samples in addition to the study of factors affecting the activation of immunity.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

**Source of Funding:** Self

**Ethical Clearance:** There is no violation of human rights and environmental pollution

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