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## Assessment of Interleukin\_10 level in Sudanese Patients with Chronic Lymphocytic Leukemia in Khartoum State

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#### **ABSTRACT**

**Background:** Chronic lymphocytic leukemia (CLL) is the most predominant leukemia among adults. Interleukin-10 (IL-10) secretion has potent immunosuppressive effects and it has a strong stimulating impact on B-lymphocytes, inducing proliferation and differentiation. This study was conducted to investigate the serum levels of IL-10 in patients with CLL (cases) and comparing them with apparently healthy age and gender match volunteers as control group.

**Method:** A total of 88 blood samples were randomly collected. 44 blood samples were withdrawn from cases, while the rest were obtained from control. Serum samples after centrifugation of blood were obtained for IL-10 level evaluation. Human IL-10 ELISA max Deluxe kit was used to determine IL-10 in each sample following manufacture instructions. The Data was analyzed through statistical package for the social science (SPSS) version 20.

Results: Our results showed that the mean of IL\_10 level among CLL patients ( $22.7\pm5.34$  pg/ml) was significantly higher (P-value: 0.002) than the mean of IL\_10 level among control group ( $4.99\pm0.55$  pg/ml). Among case groups females showed IL-10 mean of  $29.09\pm10.85$  pg/ml that was significantly higher than male's  $18.22\pm5.04$  pg/ml with p-value 0.023. Our result finds no significant difference between cases below 55years ( $23.62\pm8.03$  pg/ml) and above 55 years ( $22.07\pm7.19$  pg/ml) in the level of IL-10 with P-value 0.893.

**Conclusion:** In conclusion, this study determined higher serum IL-10 levels in CLL patients compared with healthy controls. Gender and duration of disease have significant effect on serum IL-10 level among CLL cases. However, sample size in this study was small and larger scale research is needed in this field with the inclusion of several factors such as disease, grade and outcome.

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## **List of Abbreviations IL-10:** Interlukin-10

CLL: Chronic Lymphocytic leukemia

Background

Chronic lymphocytic leukemia (CLL) is identified with bulk of mature-appearing lymphocytes in the blood, marrow, spleen, and lymph nodes. Based on International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria A minimum of 5000 circulating B cells/µl are required for presumptive diagnose of CLL, however, it should be confirmed by locality demonstration by using flowcytometry. About 25% of cases are asymptomatic

and are identified by chance on clinical or laboratory examination. CLL Patient could express weight loss, weakness, and fatigue and infections recurrences. Symptoms associated to thrombocytopenia or anemia may also been occurred. Generalized lymphadenopathy is the most predominant clinical feature; however, mild to moderate splenomegaly is present in two-thirds of patients [1-3].

In general population most CLL cases are elderly (median age 71.5 years). At time of diagnosis the median age is younger in males (70 years) compared to the females (73 years), with the male: female ratio being 1.3:1 Moreover, there was a high occurrence of CLL in the West part of the world, however, the disease is much less commonly seen in some other parts of the world, especially, Japan and China [4-6].

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In Sudan, CLL is observed mainly in adults (median age  $\sim$ 60 years). It's represented 21.7% of all leukemia cases in Sudan, and the second most frequent in male's population 24.6% and the least observed leukemia in females 17.6% [7].

Interleukin 10 (IL-10), also called human cytokine synthesis inhibitory factor (CSIF), is an anti-inflammatory cytokine. IL-10 in human is encoded by the IL10 gene (8). Originally, IL-10 was thought to be secreted only by T helper-2 (Th2) cells, but recently it is known to be made by a multiple cell types including B-lymphocyte. IL-10 is a cytokine with various, multidirectional, effects in immunoregulation and inflammation. IL-10 secretion has potent immunosuppressive impact through inhibition of Th1 type cytokines, including interferon-gamma and IL-2 (9). IL-10 has strong stimulating impacts on B-cells, inducing proliferation and differentiation. Interestingly, in B-cell lymphomas cell lines, IL-10 has been identified to serve as an autocrine growth factor. Therefore, it could be considered as important prognostic factors for both Hodgkin and non Hodgkin lymphoma [8-10].

To the best of our knowledge only few data are available about the serum levels of IL-10 cytokines in patients with CLL in Sudan. Therefore, this study was conducted to investigate the serum levels of IL-10 in patients with CLL and comparing them with healthy volunteer as well as study of the IL-10 relationship with demographic character along with clinical data of CLL patients.

#### Methods

## Study Design, Setting and Characteristics of Population

This study was cases control conducted on 44 Sudanese adult cases with CLL referred to Radiation & Isotopes Centre in Khartoum state, and 44 healthy controls. The study period extending from November 2020 to February 2021. The diagnosis of CLL was made based on clinical examination, morphological assessment of peripheral blood films, and bone marrow smear by aspirate examination, as well as flowcytometric immunophenotypic profile.

## **Inclusion and Exclusion Criteria**

Patients diagnosed with CLL were included as cases in this study, in contrary, healthy adult volunteers were included as controls. Any case or control with history of smoking, alcohol consumption, immunodeficient or with any kind of inflammatory disorder was excluded from this study.

## Sample Collection and Processing

A total of 88 blood samples were randomly collected. 44 samples were withdrawn from patients with CLL, while the rest were obtained from control. Four ml of blood samples have been collected from each patient and placed in plain container to obtain serum samples after centrifugation for IL-10 level measurement.

## **Evaluation of IL-10 Level**

The principle of Human IL-10 ELISA max deluxe kit (BioLegend, SanDiago, LotNo: B232253) is based on sandwitsh ELISA technology, Using VIRCELL micro plate reader system, Model V-2100C. The Procedure was done to assess the IL-10 level in each sample according to manufacture instructions [11].

## **Detection of Samples IL-10 level**

Standard curve was built up by relating each diluted standards absorbance with it corresponding concentration. Then each sample IL-10 level was measured based on this standard curve.

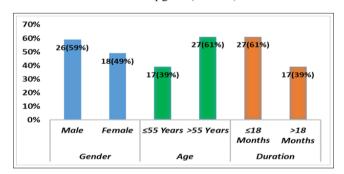
## **Data Collection and Analysis**

Structural questionnaire has been utilized to gather data from cases and controls including age, gender and clinical information of cases. Laboratory data have been collected after analyzing samples. Data was analyzed by using SPSS version 20 and results was presented by using figures and tables.

#### Result

This study was involved 88 participant, 44 were cases while the rest were controls. Among cases group 26 (59%) were males and 18 (49%) were females. 27 (61%) cases had age above or equal 55 years and duration of disease less than or equal 18 month. While 17 (39%) of them are aged below or equal 55 years and have a duration of disease more than 18 month (figure 1). In addition, cases showed age mean of  $59.79\pm7.41$  years (ranging 48-76 years). The mean of disease duration among all cases was  $17.75\pm13.90$  months (ranging 4-120 month) (Table 1).

Our result showed that cases IL-10 mean 22.7±5.34 pg/ml was significantly higher than controls mean 4.99±0.55 pg/ml with P-value 0.002 (Table 2). Among cases group females showed IL-10 mean of 29.09±10.85 pg/ml that was significantly higher than males IL-10 mean 18.22±5.04 pg/ml with p-value 0.023 (Table 3). Our result also finds no significant different between cases below 55years (23.62±8.03 pg/ml) and above55 years (22.07±7.19 pg/ml) in the level of IL-10 with P-value 0.893 (Table 3). However, Duration of disease have significant effect on the cases IL-10 level pg/ml with P-value 0.012. Cases with durations of disease less than 18 month have IL-10 mean of 19.37±6.00 pg/ml which is lower than that of cases with duration of disease more than 18 Months means 27.90±10.12 pg/ml (Table 3).



**Figure 1:** Shows Demographic Character of Case Along With Their Duration of Disease

**Table1:** Show Cases Age/Years and Duration of Disease (Mean, Standard Deviation, Minimum, Maximum)

Variables	Mean±SD	Maximum	Minimum
Age (Years)	59.79±7.41	76.00	48.00
Duration (Months)	17.75±13.90	120.00	4.00

Table 2: Comparison between Cases and Controls in the Result of IL-10 pg/ml By Using Independent T test

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Parameters	Group	Mean±SD	P-value	
IL10 pg/ml	Case	22.7±5.34	0.002	
	Control	4.99±0.55		

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Table 3: Show Comparison between Cases in IL-10 level (pg/ml) According To the Gender, Age/Years and Duration of Disease

Variables	Gender	N	IL-10 Mean±SD	P-value
Gender	Males	26	18.22±5.04	0.023
	Females	18	29.09±10.85	
Age	≤55 Years	17	23.62±8.03	0.893
	>55 Years	27	22.07±7.19	
Duration	≤18 Months	27	19.37±6.00	0.012
	>18 Months	17	27.90±10.12	

## Discussion

In this study we investigate the correlation between IL-10 level and CLL. We involved 44 cases and 44 controls. The mean age of cases was 59.79±7.41 years (ranging 48–76 years) and this was comparable to Amar et al., finding in Sudan whom reported that CLL is found to be occurred mainly in adults (median age~60 years) [7]. And also agreed with finding of several other studies whom conclude that CLL is primarily disease of elder adults with over 95% of patients aged above 50 years with a median age of 70 years at the time of diagnosis (12, 13). Moreover, among 44 randomly selected cases male were more predominant than female and this was agreed with Siegel et al., finding whom reported that CLL is slightly more common in males, with a 1.25:1 male: female ratio [12-14].

In this study, cases had IL-10 level higher significantly than controls. Several studies also demonstrate a significant increase in IL-10 levels of CLL patients compared to healthy controls. In addition, various studies reported that elevated levels of IL-10 in CLL were associated with poor prognosis. Such elevation in the IL-10 level could be due to its secretion by cancer cells or by various cells of the immune system, including T and B-lymphocytes, macrophages and monocytes [15-20]. Interestingly, in B-cell lymphomas cell lines, IL-10 is serving as an autocrine growth factor. Serum IL-10 levels have been demonstrated to be important prognostic factors for both Hodgkin and non Hodgkin lymphoma [9,10].

In this study age have no effect on the serum level of IL-10 among CLL patients. On the other hand an elevated level of serum IL-10 have been observed among females population compared to the males and the later point may need more investigation in the future studies to roll out the underline factors. Cases with duration of disease over 18 month had shown a higher IL10 level than those below 18 month, this is not surprising because by increasing duration of disease may result in more IL-10 production from malignant cell which serve as autocrine growth factor [9,10] leading to proliferation of more malignant cell which then repeat the cycle. This cycle can only been broken by starting therapy [20].

## Conclusion

In conclusion, the recent study showed a higher serum IL-10 level in CLL patients compared to the healthy controls. Gender and duration of disease have significant effect on serum IL-10 level among CLL cases. However, our sample size is small and larger scale studies with inclusion of several factors such as disease grade and outcome are needed in this field. In addition, further studies about the biological effect of high IL-10 levels on the pathogenesis or progression of chronic lymphocytic leukemia is clearly warranted.

## Declarations

Ethics approval and consent to participate Prior to conduct the study a verbal consent has been taken from each participant in this study.

## Consent for publication

Not applicable.

## Availability of data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## **Competing interests**

The authors declare that they have no competing interests

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The authors received no specific funding for this work.

## Authors' contributions

WI, BM, and RH were responsible for the statistical analysis, and interpretation of the data, and the drafting of the manuscript. WI, RH, MM, MA, and IK and were responsible for the conception and design of the study, analysis and interpretation. BM revise the final draft of manuscript. All authors read and approved the final manuscript.

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