Original article

CD38 and ZAP-70 as prognostic immunological parameters in patients with chronic lymphocytic leukemia

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Abstract

Background: Several immunological parameters have been investigated in patients with chronic lymphocytic leukemia (CLL). Some of them are important in detecting the prognosis of the disease.

Objectives: the aim of this study was to evaluate the level of ZAP-70 and CD38 in patients with newly diagnosed chronic lymphocytic leukemia.

Materials and methods: The study was done on 50 patients with newly diagnosis CLL 36 male and 14 female. CD38 and ZAP-70 were measured in patients by using flow cytometry. These patients were divided according to Ria stage into 29 patients with group II, 21 patients with group I, group I included Rai stage O, I, II in which the RBC and platelet counts are normal while group II included Rai stage III and IV in which RBC and platelet count are low.

Results: ZAP-70 and CD38 were significantly increased in patients with group II when compared to group I. ZAP-70 and CD38 may be regarded as bad prognosis factor for CLL patients.

Conclusion: From the results of the current study, we conclude that ZAP-70 and CD38 high level in patients with chronic lymphocytic leukemia is associated with bad prognosis

Keywords: CD38, ZAP-70, CLL

Introduction

Chronic lymphocytic leukemia is the most common lymphoid malignancy, it is a disease predominantly seen in elderly with the incidence twice higher men [1]. CLL showed familial tendency with 3-8 times higher than in normal population [2].Chronic lymphocytic leukemia characterized by accumulation of terminally different clonal of CD5+ B-cell from proliferation and differentiation in the bone marrow and secondary lymphoid organ. It is the most common type of malignancy in the western world but its incidence is low in Far East [3]. Chronic lymphocytic leukemia has different prognosis where the disease may be growing slowly with minimal changes in blood cell count; other may have a faster growing malignancy [4].

ZAP-70 is a member of the tyrosine kinase group of protein and is normally showed in T-cell and natural killer cells (NK). ZAP-70 have a vital role in the regulation of normal T-cell functions, such as T-cell receptor(TCR),signal initiation, T-cell activation, cell migration and apoptosis [5].

The expression of ZAP-70 (> or = 20% of B cell) has showed to associated with increased risk for bad prognosis in patients with CLL and is regarded as great risk factor in those patients [6].

CD38 is glycoprotein with small cytoplasmic region (21 amino acids), a single chain transmembrane region (23 amino acids), and 256 amino acid extracellular domain that can be loosely divided into two regions. The extracellular amine protein consists of 156 amino acids that make up 5 α-helices. This region is adjacent to the COOH domain (amino acids 200-300) that contains four parallel P-sheets surrounded by two long and two short α-helices [7].CD38 expression on the leukemic cell regarded as an excellent prognostic indicator because it's measured from peripheral blood sample easily [8]. Furthermore, measurement of CD38 expression arrows the identification of sub group of patients with better prognosis within a presumably poor prognostic and the detection of patients with poor prognosis among what is considered better prognostic group [9].

Materials and methods:

This study was done of 50 patients with newly diagnosed chronic lymphocytic leukemia from March 2013 till March 2015 included 36 male and 14 female, the age of the patients rage from 45-75 years, all of the patients were diagnosed morphologically as chronic lymphocytic leukemia. These patients were attending Medical City in Baghdad, National Center of Haematology (University of Mustansyria), Al-Yarmouk Teaching Hospital and Al-Emammain kadhumain Medical City.

Those patients were divided into two groups according to Rai staging group I included Rai stage O, I, II in which the RBC and platelet counts are normal while group II included Rai stage III and IV in which RBC and platelet count are low. ZAP-70 and CD38 were determined in patients of the above group by flow cytometry method using Four-Colour Cyflow®

Statistical analysis: Data were expressed; Student's t-test was used to evaluate differences between the studied groups. For all test, P≤0.05 was considered statistically significant. Analysis of data was carried out using the available statistical package of SPSS-22 (Statistical Packages for Social Sciences-version 22).

Results :

Table (1) and figure (1) represent the comparison of the mean value of ZAP-70 in patients of group I and group II chronic lymphocytic leukemia.

The ZAP-70 level in patients with group II chronic lymphocytic leukemia was significantly increased (p=0.0001) when compared to group I.

Table (2) and Figure (2) represents the comparison of the mean value of CD38 concentration in the sera of group I and group II chronic lymphocytic leukemia.

CD38 value were significantly increased (p=0.001) in patients with group II chronic lymphocytic leukemia when compared to group I.

**Table (1): levels of ZAP-70 in group I and II chronic lymphocytic leukemia**

		Group I (n=21)	Group II (n=29)
ZAP-70	Mean ± SD	8.82±17.10	37.58±22.29
	Standard Error of Mean	3.73	4.14
	Range	0.19-61.97	1.22-87.04
	50th (Median)	0.90	24.49
	P value	0.0001*	
*Significant difference means using Student-t-test for difference between two independent means at 0.05 level.			

Table (2): level of CD38 in patients with CLL group I and II

		Group I (n=21)	Group II (n=29)
CD38	Mean ± SD	6.25±9.30	36.01±24.60
	Standard Error of Mean	2.03	0.574
	Range	0.53-39.28	0.96-78.92
	50th (Median)	2.49	28.64
	P value	0.0001*	
*Significant difference means using Student-t-test for difference between two independent means at 0.05 level.			
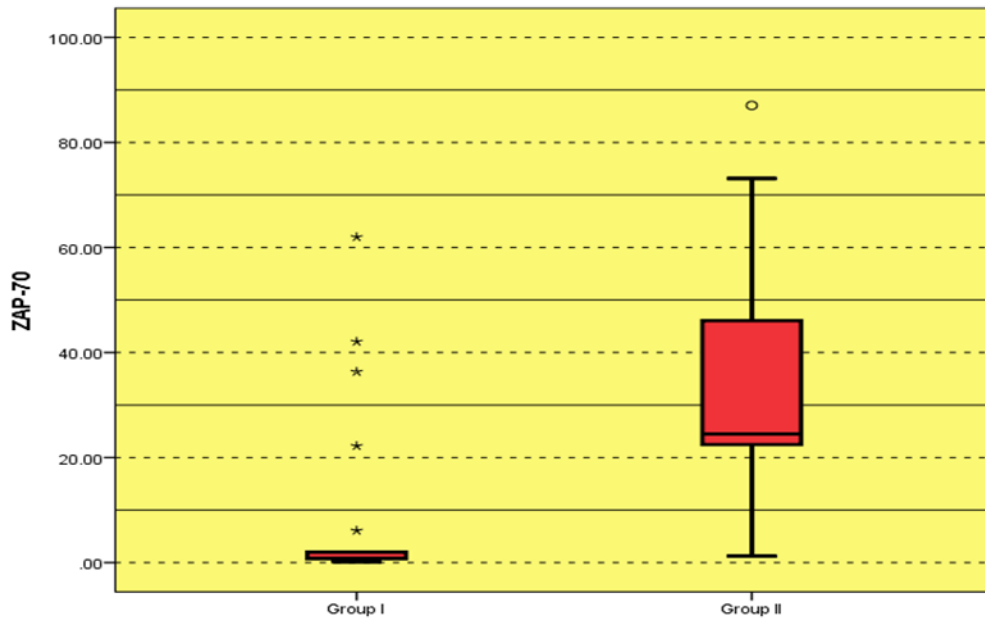
Figure (1): Distribution of ZAP-70 (mean±SD) in patients with chronic lymphocytic leukemia group I and II
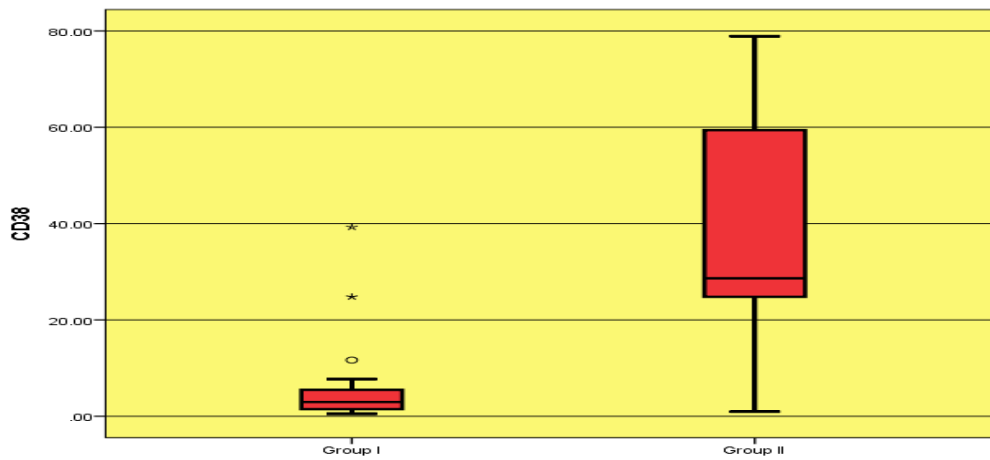
Figure (2): Distribution of CD38 (mean ± SD) in patients with chronic lymphocytic leukemia group I and II

Discussion

There are many immunological parameters used to determine the prognosis at the time of diagnosis of CLL that would help the decision about treatment and to determine the outcome of the disease [10].ZAP-70 is a member of the family of intracellular tyrosine kinases, is significantly expressed in normal T cells. It is also may be express at early stage of chronic lymphocytic leukemia [11]. The result in the present study determine that ZAP-70 might be useful for detecting the prognosis of the disease because the level of ZAP-70 increase in patients with group II chronic lymphocytic leukemia when compared to group I chronic lymphocytic leukemia patients. The data in our study regarding ZAP-70 value agreed with previous result which indicate that ZAP-70 in patients with chronic lymphocytic leukemia increase as the disease progress [12]. CD38 is a protein that have many function belongs to the number of molecules independently as ecto-enzymes as receptors, CD38 may split the patients with chronic lymphocytic leukemia into two groups and represent a dependable negative prognostic factor [13]

Regarding CD38, the data in this study showed that it might be useful for prognosis of the disease since the value of CD38 increase as the disease progress and patients with CD38 high value may be regarded bad prognosis for the patients in chronic lymphocytic leukemia [13].This observation agreed with previous results which indicate that expression of CD38 patients with CLL is associated with bad prognosis and poor outcome [14].

Conclusion

From the results of the current study, we conclude that ZAP-70 and CD38 high level in patients with chronic lymphocytic leukemia is associated with bad prognosis.

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CD38 وZAP-70 معلمات مناعية للتكهن في المرضى الذين يعانون من سرطان الدم الليمفاوي المزمن

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الملخص

الخلفية : هناك عدة انواع من المعلمات المناعيه نم دراستها في مرضى ابيضاض الدم اللمفاوي المزمن .بعض من هذه المعلمات مهمه في تعيين حالة المريض.

الاهداف :اجريت هذه الدراسه لمعرفة فائدة ZAP-70 و CD38 في مرضى ابيضاض الدم اللمفاوي المشخصين حديثا.

المواد والطرق : تم اجراء هذا البحث على 50 مريضا 36 ذكور و14 اناث، حيث تم قياس ZAP-70 و CD38 في مصول هؤلاء المرضى بواسطة جهاز الفلوسايتومتري. تم تقسيم هؤلاء المرضى الى قسمين المجموعه الاولى تضم (21) مريض والثانيه تضم (29) مريض**.**

النتائج : لقد كانت هناك زياده محسوسه في مستوى ZAP-70 و CD38 في مصول مرضى المجموعه الثانيه مقارنه بالمجموعه الاولى وبذلك بين اهميه ال ZAP-70 و CD38 كمعلمات لسؤء حالة المريض المصاب بابيضاض الدم اللمفاوي.

الاستنتاج : من نتائج الدراسة الحالية، فإننا نستنتج أن هناك ارتباط بين ZAP-70 و CD38 على مستوى عال في المرضى الذين يعانون من سرطان الدم الليمفاوي المزمن مع المسيرة السيئة لهذا المرض.

الكلمات الرئيسية: ZAP-70 وCD38 , سرطان الدم الليمفاوي المزمن