

## Abstract

This study was carried out on 41 newly diagnosed chronic lymphocytic leukemia (CLL) patients for investigation of the diagnostic value of CD49d and its correlation with disease outcome in CLL patients. CD49d expression on CLL cells in peripheral blood samples was estimated by flow cytometry analysis. Patients with  $\geq 31.5\%$  of neoplastic cells expressing CD49d were considered high CD49d cases. The cases with high CD49d expression were significantly associated with progression to a more advanced stage while lymphocytic doubling (LD) and mortality were not significantly associated with high CD49d expression. Lymphocytic doubling time (LDT) was significantly shorter in high CD49d versus low CD49d of CLL patients. Additionally, high CD49d group showed with  $p < 0.05$  significantly between both high CD49d and low CD49d of CLL patients. Multivariate analysis revealed that CD49d is an independent prognostic factor for predicting lymphocytic doubling time. Moreover, the advanced Rai stage and high CD49d are independent prognostic factors for shorter progression free survival. Overall, CD49d is selected as the most important flow cytometry-based prognostic biomarker regardless of other prognosticators such as CD38 and ZAP-70. Consistently, bivariate analysis revealed that CD49d identified CLL patients with poorer outcome independent of CD38 and ZAP-70. Overall, CD49d acts as an independent bad prognostic marker for B-CLL patients at different stages and a predictor of overall survival.

**Keywords:** CD49d, CLL, flow cytometry, prognostic biomarker, lymphocytic doubling time, progression free survival, overall survival.

**Introduction:** Chronic lymphocytic leukemia (CLL) is a type of cancer that affects the white blood cells. It is characterized by the presence of a large number of abnormal lymphocytes in the blood and bone marrow. The disease is often diagnosed in older adults and can progress slowly over time. The prognosis of CLL varies depending on the stage of the disease and the presence of certain biomarkers. CD49d is a cell surface protein that is expressed on CLL cells. It has been shown to be associated with disease progression and poor outcome. This study aims to investigate the diagnostic value of CD49d and its correlation with disease outcome in CLL patients.

**Methods:** This study was carried out on 41 newly diagnosed CLL patients. The expression of CD49d on CLL cells was estimated by flow cytometry analysis. Patients with  $\geq 31.5\%$  of neoplastic cells expressing CD49d were considered high CD49d cases. The cases with high CD49d expression were significantly associated with progression to a more advanced stage while lymphocytic doubling (LD) and mortality were not significantly associated with high CD49d expression. Lymphocytic doubling time (LDT) was significantly shorter in high CD49d versus low CD49d of CLL patients. Additionally, high CD49d group showed with  $p < 0.05$  significantly between both high CD49d and low CD49d of CLL patients. Multivariate analysis revealed that CD49d is an independent prognostic factor for predicting lymphocytic doubling time. Moreover, the advanced Rai stage and high CD49d are independent prognostic factors for shorter progression free survival. Overall, CD49d is selected as the most important flow cytometry-based prognostic biomarker regardless of other prognosticators such as CD38 and ZAP-70. Consistently, bivariate analysis revealed that CD49d identified CLL patients with poorer outcome independent of CD38 and ZAP-70. Overall, CD49d acts as an independent bad prognostic marker for B-CLL patients at different stages and a predictor of overall survival.

**Results:** The results of this study show that CD49d expression is significantly associated with disease progression and poor outcome in CLL patients. High CD49d expression was associated with progression to a more advanced stage, shorter lymphocytic doubling time, and shorter progression free survival. Additionally, high CD49d expression was associated with shorter overall survival. Multivariate analysis revealed that CD49d is an independent prognostic factor for predicting lymphocytic doubling time. Moreover, the advanced Rai stage and high CD49d are independent prognostic factors for shorter progression free survival. Overall, CD49d is selected as the most important flow cytometry-based prognostic biomarker regardless of other prognosticators such as CD38 and ZAP-70. Consistently, bivariate analysis revealed that CD49d identified CLL patients with poorer outcome independent of CD38 and ZAP-70. Overall, CD49d acts as an independent bad prognostic marker for B-CLL patients at different stages and a predictor of overall survival.

**Conclusion:** CD49d is an independent prognostic biomarker for CLL patients. High CD49d expression is associated with disease progression and poor outcome. CD49d is an independent prognostic factor for predicting lymphocytic doubling time. Moreover, the advanced Rai stage and high CD49d are independent prognostic factors for shorter progression free survival. Overall, CD49d is selected as the most important flow cytometry-based prognostic biomarker regardless of other prognosticators such as CD38 and ZAP-70. Consistently, bivariate analysis revealed that CD49d identified CLL patients with poorer outcome independent of CD38 and ZAP-70. Overall, CD49d acts as an independent bad prognostic marker for B-CLL patients at different stages and a predictor of overall survival.

**Citation:** Abdel-Aziz AF, Yahya RS, Abdel-Messih HM, Ata AM (2019) Diagnostic Value of CD49d Expression in Patients with Chronic Lymphocytic Leukemia. *Biochem Physiol* 8: 249. doi: [10.4172/2168-9652.1000249](https://doi.org/10.4172/2168-9652.1000249)

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Figure 3: A receiver operating curve (ROC) analysis of CD49d levels.

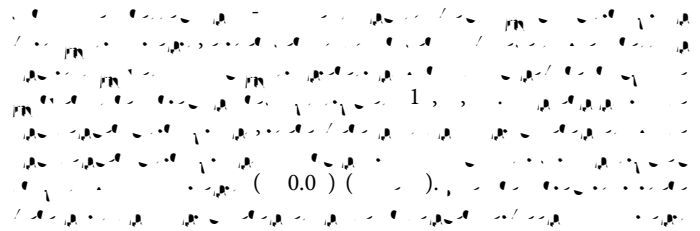


Figure (4B): Patient with low CD49d expression on B-CLL cells (8.24%).

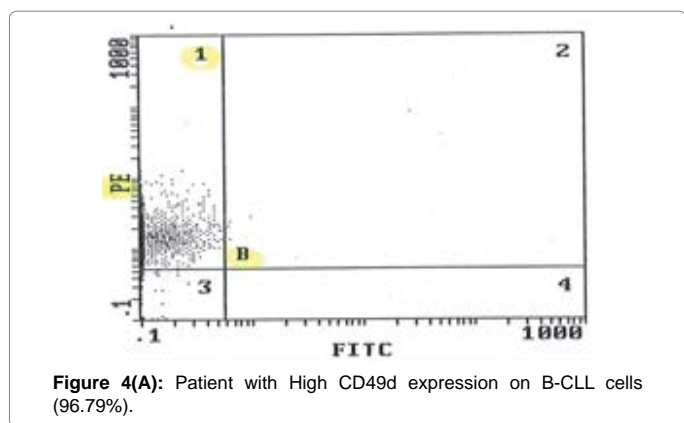


Figure 4(A): Patient with High CD49d expression on B-CLL cells (96.79%).

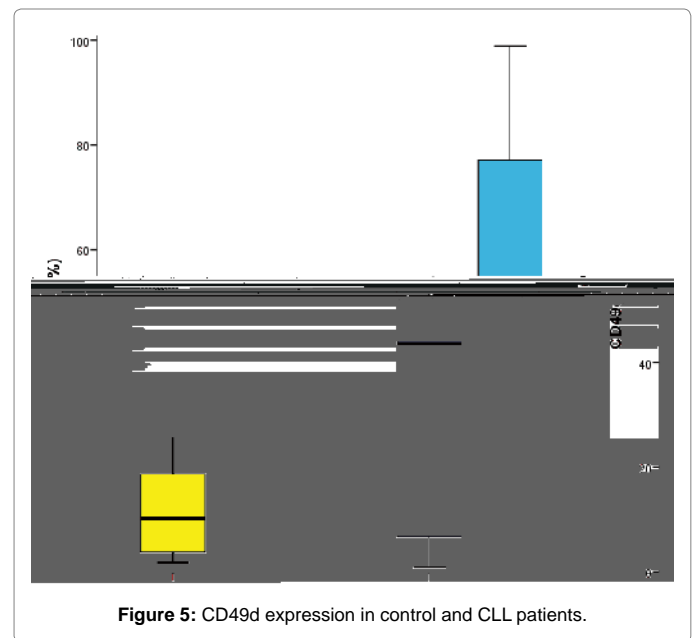


Figure 5: CD49d expression in control and CLL patients.

		CD49d <sup>low</sup>	CD49d <sup>high</sup>	P
		N=18	N=23	
Age (Years)	Median	57.5	59	0.285
	Range	45-69	48-84	
Gender	Males, N (%)	17 (94.4%)	17 (73.9%)	0.112
	Females, N (%)	1 (5.6%)	6 (26.1%)	

Age is presented by median and range. Gender is presented by number and percentage. Significance probability when P < 0.05.

Table 6: Age and gender distributions according to CD49d positivity in studied groups of CLL patients

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