



TLE1 gene expression in adult T-cell acute lymphoblastic leukemia

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Background

Transducin-like enhancer of split 1 (TLE1) is a member of the TLE family of transcriptional co-repressors that control the transcription of a wide range of genes.

Objective

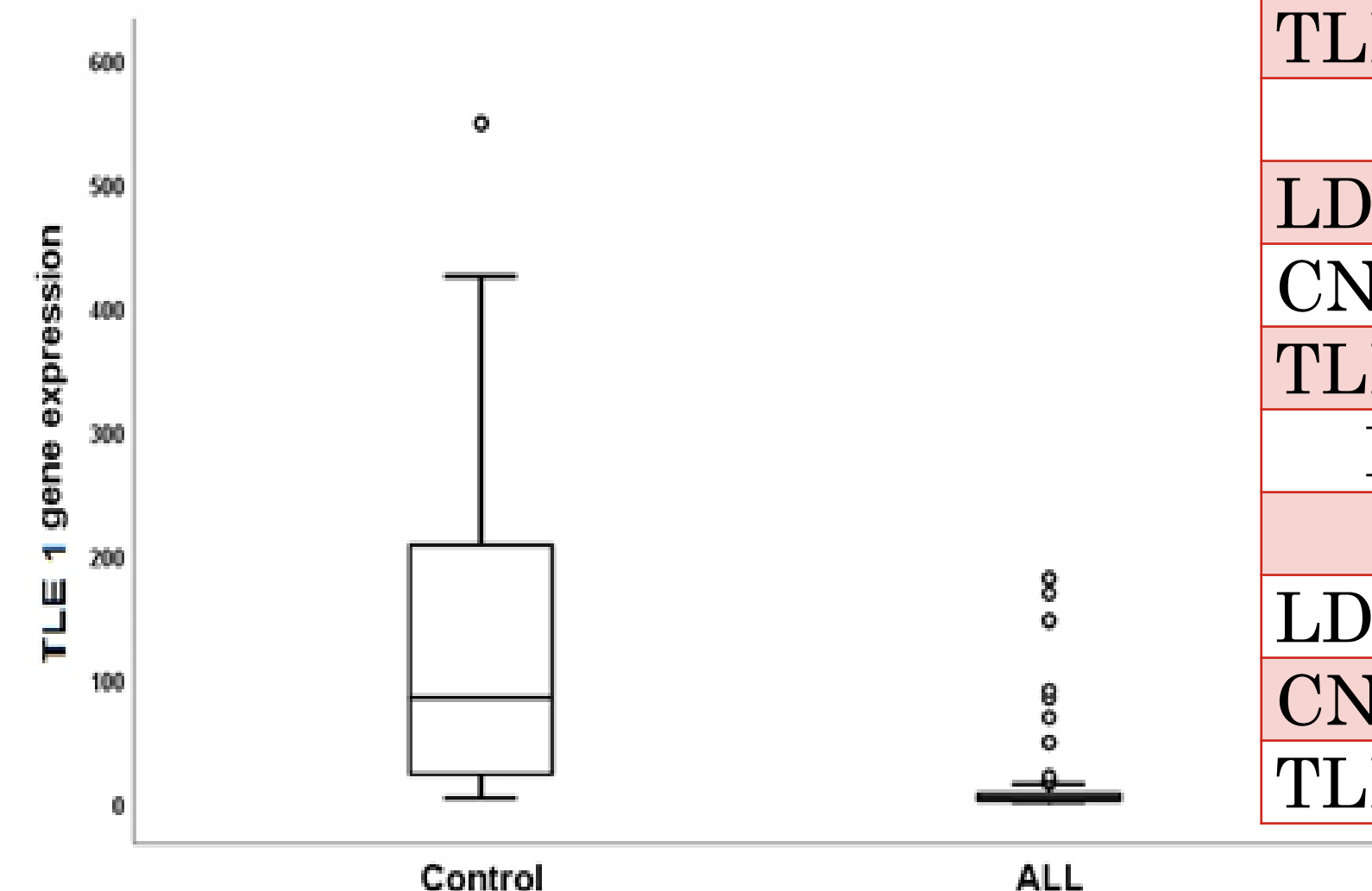
The aim of this study was to evaluate the prognostic role of TLE1 gene expression in patients with T-cell acute lymphoblastic leukemia (T-ALL).

Materials & Methods

97 newly diagnosed T-ALL patients admitted to the Mansoura University oncology center (59 males and 38 females) with median age (33 years) in addition to 102 apparently healthy individuals served as a control group. TLE1 gene expression was measured in both patients and control groups by real time – PCR. The calculation of relative gene expression was done using the $\Delta\Delta C_t$ method.

Results

TLE1 gene expression was significantly down regulated in T-ALL cases (median TLE1 expression: 2.83) as compared to controls (median TLE1 expression : 84.65) ($P < 0.001$)



	Low TEL1 (N=49)		High TEL1 (N=48)		p
ETP-ALL/LBL	16	32.6%	9	18.7%	0.04
CNS infiltration	27	51%	3	6.2%	0.001
Remission	23	46.9%	46	95.8%	<0.001
Non remission	26	53.1%	2	4.2%	
Relapse	6	12.2%	3	6.3%	0.023

low TEL1 gene expression was significantly associated with Early T cell precursor (ETP)-ALL/LBL subtype, higher frequency CNS infiltration, non-remission and higher relapse rate ($P = 0.04$, < 0.001 , < 0.001 and 0.023 respectively). No significant differences were found between low and high TEL1 expression regarding age, gender, TCR rearrangement or any laboratory data.

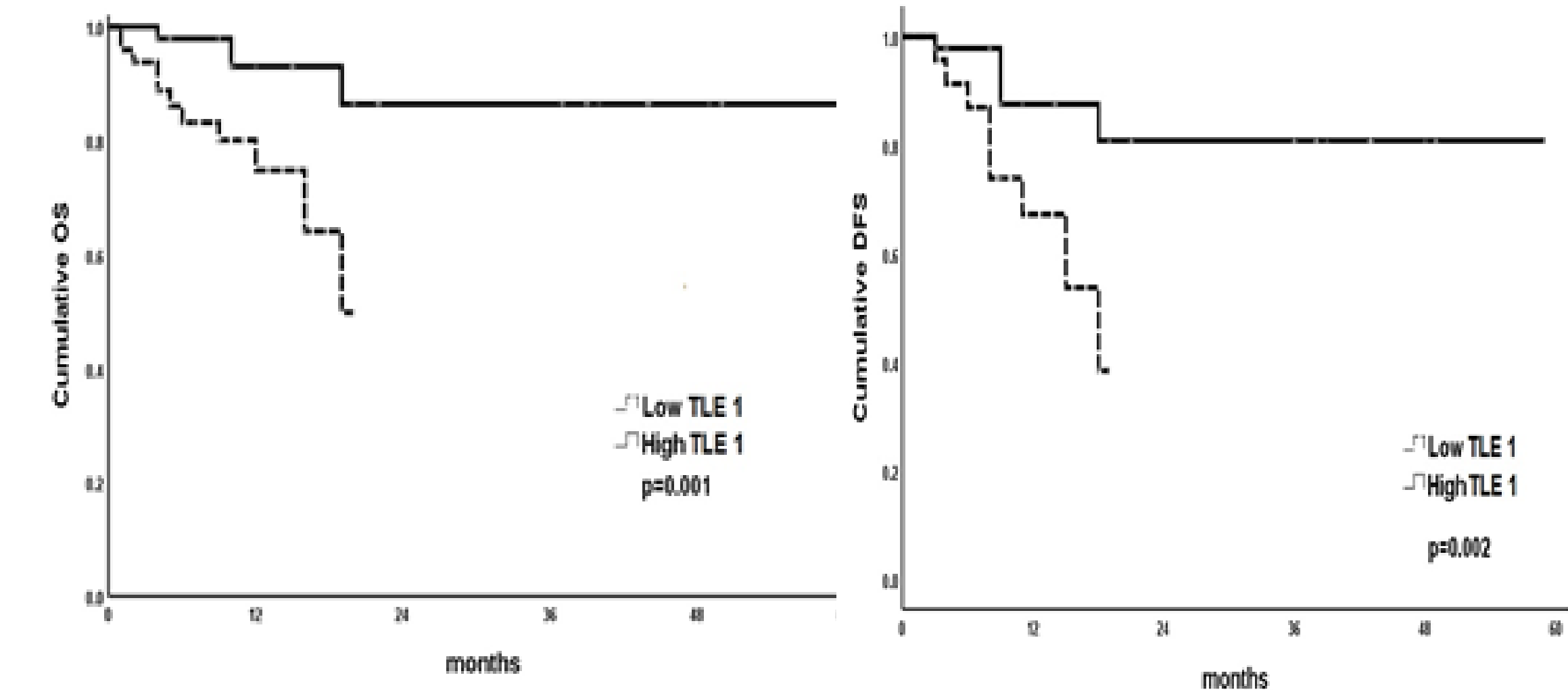
	P value	HR (95% CI)
Cox regression analysis for prediction of OS		
LDH	0.029	1.034(1.003-1.076)
CNS infiltration	0.036	2.986(1.077-8.279)
TLE1	0.012	0.702(0.533-0.925)
Cox regression analysis for prediction of DFS.		
LDH	0.413	1.023(0.947-1.079)
CNS infiltrations	0.024	3.218(1.164-8.901)
TLE1	0.011	0.746(0.595-0.936)
Logistic regression analysis for prediction of Relapse.		
	p	HR (95% CI)
LDH	0.192	0.993(0.988-1.012)
CNS infiltration	0.265	1.551(0.717-3.354)
TLE1	0.032	0.774(0.591- 0.913)

low TEL1 gene expression was associated with significantly shorter OS in univariable analysis ($P=0.012$). However, in multivariable analysis, only down regulated TEL1 gene expression was considered as poor prognostic factor for shorter OS ($P=0.006$)

low TEL1 gene expression were considered as poor prognostic factors for shorter DFS in both univariable ($P= 0.011$) and multivariable ($P= 0.002$). .

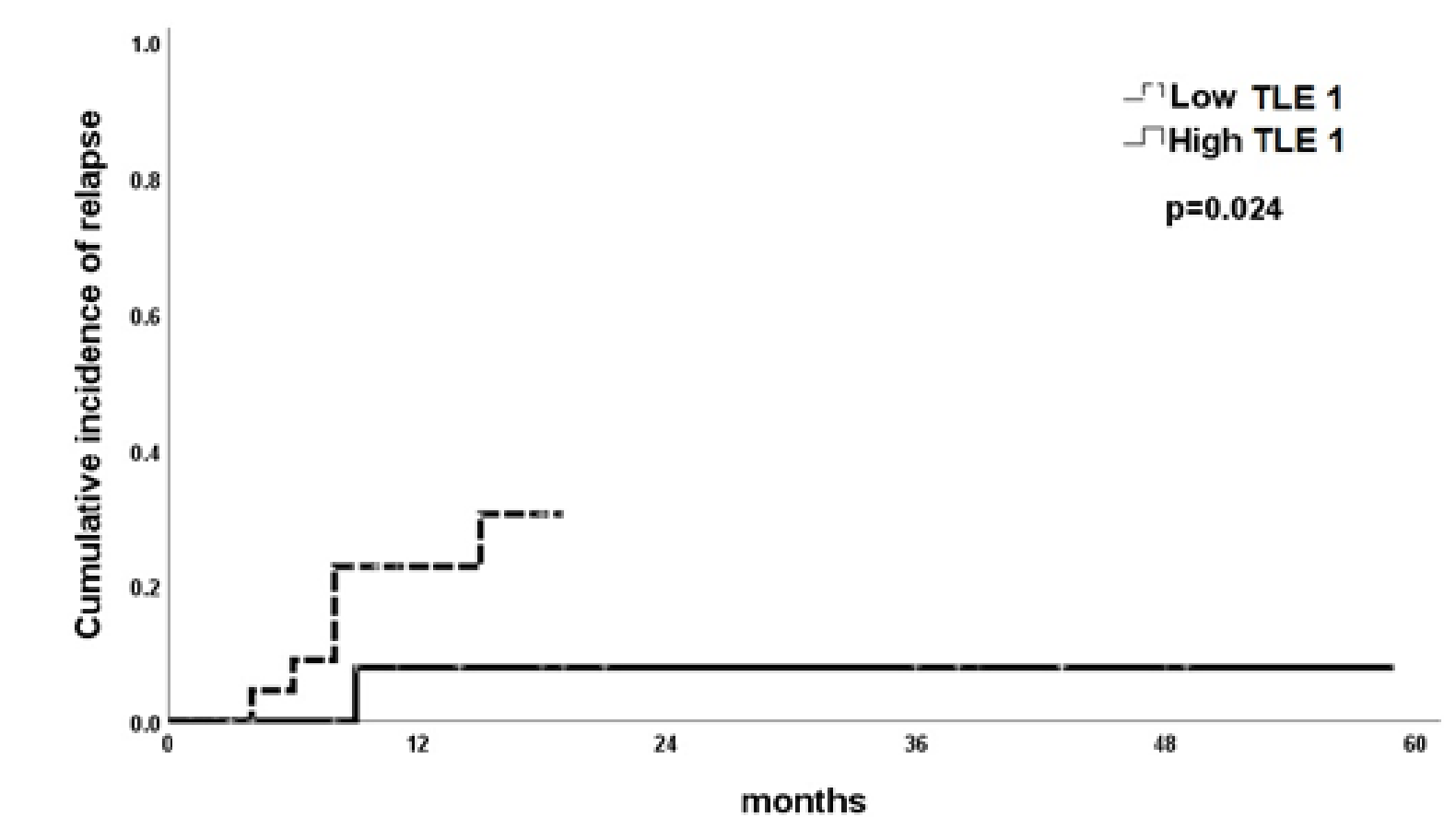
	P value	HR (95% CI)
Cox regression analysis for prediction of OS		
LDH	0.936	1.043(0.957-1.342)
CNS infiltration	0.098	0.35 (0.1-1.2)
TLE1	0.006	0.619 (0.44-0.872)
Cox regression analysis for prediction of DFS.		
LDH		
CNS infiltrations	0.002	1.028(1.003-1.262)
TLE1	0.002	0.373(0.201-0.693)
Logistic regression analysis for prediction of Relapse.		
LDH		
CNS infiltration		
TLE1	0.021	0.803(0.609-0.96)

Low TEL1 gene expression was considered as risk predictors of relapse in univariable ($P= 0.032$) and multivariable ($P=0.021$)



T-ALL patients with low TLE1 expression have short OS and shorter DFS as compared to subgroup of T-ALL patients with high TEL1 group ($P0.001$; 0.002 respectively).

CIR was significantly higher subgroup of T-ALL patients with low TEL1 expression as compared to those with high TEL1 expression ($P=0.024$) (Figure 3).



Summary

TLE1 gene expression was significantly down regulated in T-ALL as compared with controls. Low TLE1 expression is independent predictor of the T-ALL patient's outcome and could open way for further risk stratification and targeted therapy in T-ALL.

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