PROGNOSTIC VALUE OF CTBP2 AND CASP8AP2 EXPRESSION IN ADULT ACUTE B-CELL LYMPHOBLASTIC LEUKEMIA PATIENTS

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Introduction

Acute lymphoblastic leukemia is a clonal proliferation of the lymphocyte precursor cells. Both T-cell and B-cell precursors can give rise to ALL. Molecular markers have made a breakthrough in ALL after proving to be important in disease pathogenesis and as therapeutic targets. The C-terminal binding protein 2 (CTBP2) is a transcriptional repressor that was reported to correlate with tumorigenesis and progression in several cancers. Down-regulation of CTBP2 mediated by some tumor suppressors results in p53-independent apoptosis and reduced tumor cell migration and invasion. Caspase-8 associated protein 2 (CASP8AP2) has been recognized as a key mediator of apoptosis. Previous studies conducted stated that low expression of CTBP2 and CASP8AP2 gene was associated with relapse in childhood B-ALL. Yet, minimal studies have been conducted to evaluate the prognostic role of CTBP2 and CASP8AP2 gene expression in adult B-ALL.

Aim of the Work

The aim of this study was to investigate the expression of CTBP2 and CASP8AP2 genes in newly diagnosed cases of acute B-cell lymphoblastic leukemia in adult patients in relation with other clinicopathological parameters.

Subjects and Methods

SUBJECTS: This study was conducted on 40 newly diagnosed adult B-cell lymphoblastic leukemia patients of both sexes admitted to Alexandria Main University Hospital and 30 healthy individuals of matching age and sex as a control group.

METHODS: Cases and controls were subjected to full history taking, thorough clinical examination and routine lab investigations including (CBC, Bone marrow aspiration, immunophenotyping for establishing diagnosis of the cases and for follow up MRD and karyotyping for the cases whenever possible). 1. Bone marrow aspirate samples were obtained. 2. According to the manufacturer's protocol total RNA was purified using the miRNeasy Mini kit (QIAGEN, Germany).

3.cDNA reverse transcription was carried out using the RevertAid first strand cDNA synthesis kit (Thermo Fisher Scientific, USA) 4.Relative quantification of CTBP2 and CASP8AP2 expression was preformed by Taqman Gene Expression Master Mix (Thermo Scientific, USA) using the Rotor-Q 3000 RT-PCR system (QIAGEN, Germany) according to the manufacturer's instructions. A normalizer target (Beta Actin as housekeeping gene for RNA) was included in the assay. The Relative gene expression was done using the comparative Ct method.

Results

Table 1: Comparison between the two studied groups according to CTBP2 and CASP8AP2 gene expression (2^–ΔΔCt)

	Cases (n = 40)	Control (n = 30)	U	P
CTBP2				
Min. – Max.	0.001 – 200.85	0.001 – 6.87	407.00*	0.022*
Mean ± SD.	6.81 ± 32.45	0.49 ± 1.41		
Median (IQR)	0.28 (0.09 – 0.61)	0.10 (0.09 – 0.16)		
CASP8AP2				
Min. – Max.	0.08 – 162.02	0.00003 – 35.75	411.00*	0.025*
Mean ± SD.	7.48 ± 27.25	3.70 ± 9.22		
Median (IQR)	0.64 (0.31 – 1.0)	0.18 (0.07 – 2.58)		

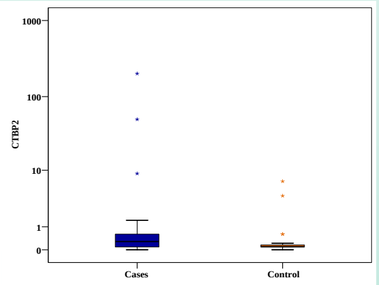

Figure 1: Box plot showing the expression of CTBP2 in both B-ALL patients and control groups.

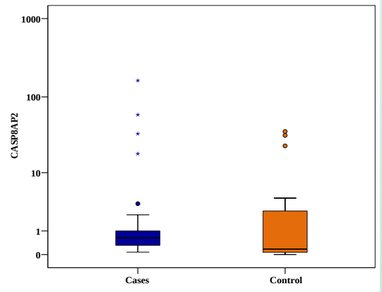

Figure 2: Box plot showing the expression of CASP8AP2 in both B-ALL patients and control groups

Table 2: Relation between CTBP2 expression levels with relapsein patients group (n = 40)

	CTBP2 ≤0.115 (n = 12) No.	%	CTBP2 >0.115(n = 28) No.	%	Test of Sig.	P
Relapse						
No	8	66.7	27	96.4	χ^2= 6.803*	FEp= 0.022*
Yes	4	33.3	1	3.6		

Table 3: Relation between CASP8AP2 expression levels with relapse in patients group (n=40)

	CASP8AP2 ≤0.301(n = 8) No.	%	CASP8AP2 >0.301 (n = 32) No.	%	Test of Sig.	P
Relapse						
No	5	62.5	30	93.8	χ^2= 5.714*	FEp= 0.046*
Yes	3	37.5	2	6.3		

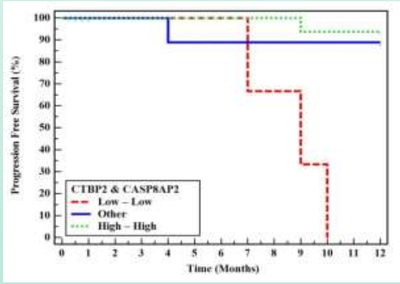

Figure 3: Kaplan-Meier survival curve for relapse free survival with CASP8AP2 and CTBP2 combined expression

Conclusion

- Low expression of CTBP2 and CASP8AP2 gene may be of value in predicting relapse in Adult B-ALL patients.
- The potential role of both genes as prognostic markers highlights their importance in clinical practice, where early identification of high-risk patients can lead to more effective management and improved outcomes in ALL.