ASSESSMENT OF EXPRESSION OF ADAM17 GENE IN ACUTE LYMPHOBLASTIC LEUKEMIA IN PEDIATRIC PATIENTS

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Introduction

Acute lymphoblastic leukemia (ALL) is a heterogeneous hematologic disease characterized by the abnormal neoplastic proliferation of immature lymphoid cells in the bone marrow, peripheral blood, and other parenchymatous organs as liver, spleen and lymph nodes. The involvement of cytogenetic, molecular as well as epigenetic diagnostic criteria in the following years have acquired a pivotal crucial and critical in the refinement of diagnosis of cases of ALL. ADAM17 (TACE) is an enzyme that impacts cancer progression through its sheddase activity, which involves cleaving cell surface proteins. This process affects growth factor signaling, angiogenesis, cell adhesion, and immune system evasion. In ALL, dysregulated ADAM17 can worsen disease outcomes by influencing cell proliferation and survival, making it a potential target for new cancer therapies

Aim of the work

The aim of this study was to define the diagnostic relevance of the expression of ADAM17 gene in newly diagnosed cases of ALL in Pediatric patients.

Patient and Methods

This study was conducted on 40 newly diagnosed pediatric ALL patients of both sexes admitted to Alexandria University Hospital and 40 individuals of matching age and sex as a control group. 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 (QIAamp RNA blood mini Kit) 3.cDNA reverse transcription was carried out using the RevertAid first strand cDNA synthesis kit (Thermo Fisher Scientific, USA) 4. Relative quantification of ADAM17 gene expression was performed using Maxima SYBR Green qPCR Master Mix (Thermo Scientific , USA) and Custom made primers were supplied by (Thermo Fisher Scientific, USA) according to the manufacturer's instructions using the Rotor-Q 3000 RT-PCR system (QIAGEN,Germany). A normalizer target (GADPH as housekeeping gene for RNA) was included in the assay. The relative gene expression was done using the comparative Ct method

Results

ADAM17 expression levels were significantly different between acute lymphoblastic leukemia (ALL) patients and the control group, with ADAM17 being overexpressed in ALL patients ($p < 0.001$). Notably, patients exhibiting lower levels of ADAM17 had a significantly higher incidence of relapse ($p = 0.01$). Conversely, those with higher ADAM17 expression levels experienced a significantly greater incidence of remission ($p = 0.007$). These findings highlight the potential role of ADAM17 as a prognostic marker in the management of ALL.

Table (1): Comparison between the two studied groups according to ADAM17 (2^–ΔΔCt):

ADAM17	Group I (n = 40)	Group II (n = 40)	U	P
Min. – Max.	0.01 – 10.10	0.01 – 4.62	382.00*	<0.001*
Mean ± SD.	3.55 ± 2.79	1.21 ± 1.05		
Median (IQR)	3.20 (1.35 – 5.38)	0.90 (0.44 – 1.44)		

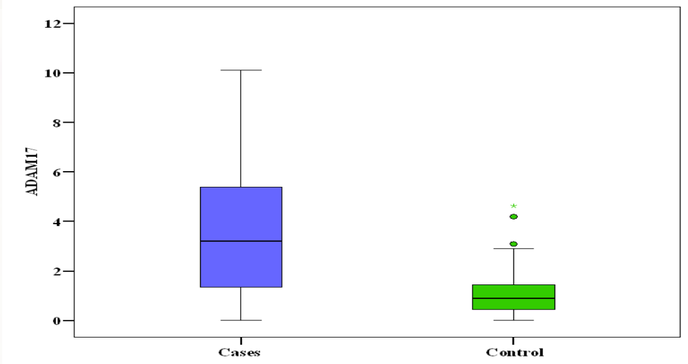

Figure (1): Box plot showing the expression of ADAM17 in both ALL patients and control groups.

Table (2): Relation between ADAM17 expression levels with patient fate in patients group (n = 40)

	ADAM17					
	Low (≤1.17) (n = 10)		High (>1.17) (n = 30)		χ^2	P
	No.	%	No.	%		
Remission	2	20.0	22	73.3	8.889*	FEp=0.007*
Relapsed	4	40.0	1	3.3	9.219*	FEp=0.010*
Died	4	40.0	7	23.3	1.045	FEp=0.418

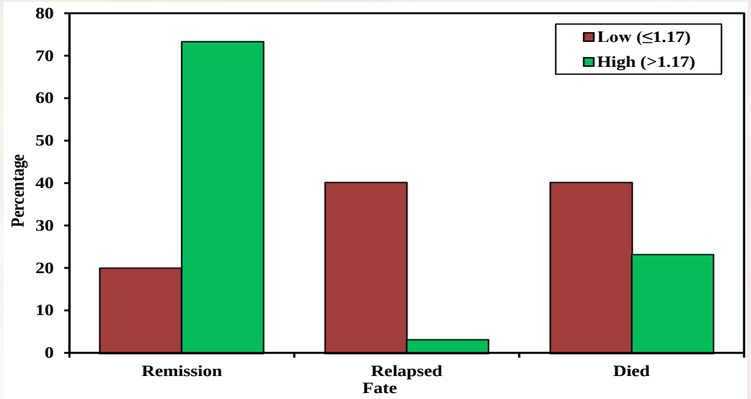

Figure (2): Bar chart relation between ADAM17 with fate in group I (Children with ALL) (n = 40)

Conclusion

The ADAM17 gene has the potential to serve as a valuable diagnostic marker in clinical practice, emphasizing its importance in the early identification of high-risk patients, which can lead to more effective management and improved outcomes in acute lymphoblastic leukemia (ALL). Low expression levels of ADAM17 may be useful for predicting relapse in pediatric ALL patients, while high expression levels could indicate a higher likelihood of achieving remission in this population.