

Introduction

Acute lymphoblastic leukemia (ALL) is the most common malignancy in pediatric age group. Despite dramatic improvements in overall survival rates, now exceeding 90% in ALL, relapse and chemoresistance persist as leading causes of treatment failure, highlighting the necessity for ongoing genomic and epigenomic research in order to refine risk stratification, therapeutic precision, and subsequently clinical outcomes. MicroRNAs are a class of short non-coding RNAs that regulate several targets, hence having a wide range of physiological as well as pathological impacts. Due to their high stability in plasma samples, miRNAs are promising blood-based biomarkers. MicroRNA-146a is turning into a noteworthy biomarker for diagnosis and prognosis of many diseases. Its principal function is regulating hematopoiesis and innate immune system functions. Numerous studies have reported that miR-146a plays a role in the initiation and persistence of neoplastic processes, however, there is limited literature on the role of miR-146a in ALL, warranting further investigation.

Aim of the Work

The aim of the work was to study the expression of miR-146a in plasma of pediatric acute lymphoblastic leukemia patients and its relation to disease characteristics.

Patients and Methods

Patients: The present work was carried out on 80 subjects including 40 newly diagnosed children with ALL and 40 healthy children of matching age and sex.
Methods:
• All subjects were subjected to full history taking, complete clinical examination, investigations including complete blood count (CBC), bone marrow aspirate examination (for patients only) and flow cytometric immunophenotyping (FCI) (for patients only).
• Quantitative determination of miRNA expression by real-time quantitative reverse transcription polymerase chain reaction (RQ-PCR).

Results

• miR-146a was significantly overexpressed in ALL patients relative to control group ($p < 0.001$).

Table 1: Comparison between the two studied groups according to plasma miRNA-146a (fold change)

	Group I (n = 40)	Group II (n = 40)	U	P
Plasma miRNA-146a (fold change)				
Min – Max	0.47 – 228.7	0.18 – 4.46	251.00*	<0.001*
Mean ± SD	16.17 ± 38.02	1.40 ± 1.15		
Median (IQR)	3.98 (1.43 – 13.29)	0.96 (0.64 – 2.26)		

IQR: Inter quartile range SD: Standard deviation U: Mann Whitney test
p: p value for comparing between the two studied groups
*: Statistically significant at $p \leq 0.05$
Group I: Children newly diagnosed with ALL Group II: Healthy children (control group)

• Patients who remained MRD-positive exhibited markedly higher median plasma miRNA-146a levels compared to MRD-negative patients

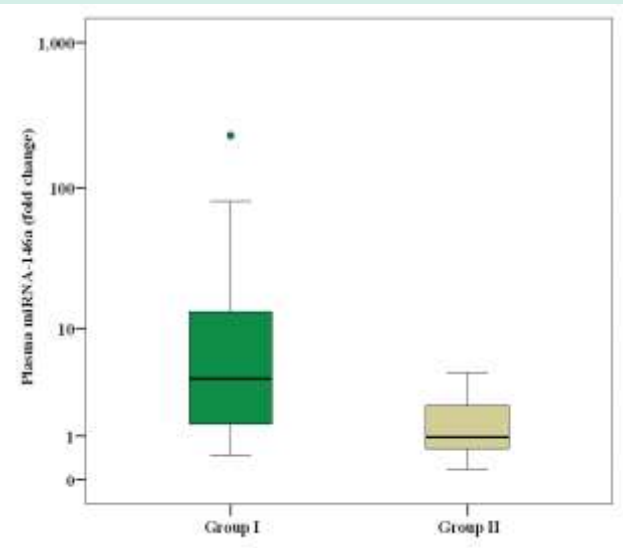


Figure 1: Comparison between the two studied groups according to plasma miRNA-146a (fold change).

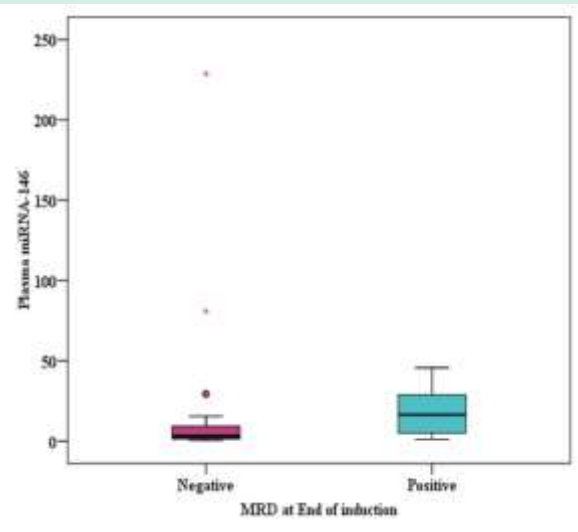


Figure 2: Relation between Plasma miRNA-146a with MRD at end of induction in group I (children newly diagnosed with ALL) (n=40).

Table 2: Relation between Plasma miRNA-146a and MRD end of induction in group I (children newly diagnosed with ALL) (n = 40)

	No.	Plasma miRNA-146a		U	P
		Mean ± SD.	Median (Min. – Max.)		
MRD at End of induction					
Negative	31	15.04 ± 42.34	3.07 (0.47 – 228.7)	69.00*	0.021*
Positive	9	20.04 ± 17.41	16.53 (1.10 – 45.70)		

SD: Standard deviation U: Mann Whitney test
p: p value for Relation between Plasma miRNA-146 with different parameters
*: Statistically significant at $p \leq 0.05$

Conclusion

miR-146a was significantly up-regulated in acute lymphoblastic leukemia patients relative to control subjects. It was also significantly over expressed in B-ALL cases relative to T-ALL cases. There was a significant association between plasma miRNA-146a levels and MRD status at the end of induction therapy. Higher levels of miR-146a were associated with positive MRD at the end of induction therapy. Hence, Elevated miRNA-146a expression may be linked to suboptimal therapeutic response or persistence of leukemic cells following induction treatment.