STUDY OF APOLIPOPROTEIN B MRNA EDITING CATALYTIC POLYPEPTIDE-LIKE 3B EXPRESSION IN PLASMA CELL MYELOMA

Myriam Abou Seif Helmy, Manal Abdelsattar Elsardy,* Neveen Lewis Mikhaael, Alaa Roshdy Elsaid Sobhy Elgreatly
Department of Clinical and Chemical Pathology, Department of Internal Hematology,* Faculty of Medicine, Alexandria University, Alexandria.

Introduction

Multiple Myeloma (MM) is a genetically and clinically heterogeneous malignancy of plasma cells that progresses through distinct stages from MGUS to advanced disease. Its pathogenesis involves complex interactions between genetic mutations, the bone marrow microenvironment, and immune dysregulation. Among the key molecular drivers, APOBEC3B has emerged as a significant contributor to MM development and progression. This cytidine deaminase enzyme promotes genomic instability through C-to -U deamination in single-stranded DNA, leading to a mutational signature frequently observed in MM. Elevated APOBEC3B expression is associated with poor prognosis, increased tumor heterogeneity, and potential resistance to therapy. Understanding the role of APOBEC3B in MM not only enhances insights into disease biology but also opens new avenues for biomarker development and targeted therapeutic strategies.

Aim of the Work

The aim of this study was to study expression of APOBEC3B in Plasma cell myeloma and correlate it with disease characteristics.

Subjects and Methods

Subjects: This study was conducted on 50 newly diagnosed plasma cell myeloma patients of both sexes, diagnosed according to the International Myeloma Working Group (IMWG) criteria. admitted to Alexandria Main University Hospital and 30 healthy individuals of matching age and sex as a control group.

Methods: All subjects underwent comprehensive medical history taking, detailed clinical examination, and routine laboratory investigations, which included complete blood count (CBC), serum albumin, serum urea, creatinine, serum calcium, serum lactate dehydrogenase (LDH), serum beta-2 microglobulin, bone marrow aspiration, and immunophenotyping to establish the diagnosis. Serum protein electrophoresis was performed only for the patient group. 1. Bone marrow aspirate samples were obtained. 2. According to the manufacturer's protocol Total RNA was extracted using the QI Aamp RNA blood mini kit (QIAGEN, Germany). 3.cDNA reverse transcription was carried out using the Revert Aid first strand cDNA synthesis kit (Thermo Fisher Scientific, USA) 4.Relative quantification of APOBEC3B 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. Patients were followed up for a period of one year, from the time of diagnosis till the end of the study, to assess response to treatment and overall survival.

Results

Table 1: Comparison between the two studied groups according to APOBEC3Bgene expression (2^–ΔΔCt)

	Patients (n = 50)	Control (n = 30)	U	P
APOBEC 3B				
Min. – Max.	0.33 – 19.29	0.19 – 4.03	167.00*	<0.001*
Mean ± SD.	6.96 ± 5.26	1.25 ± 0.82		
Median (IQR)	5.76 (2.89–9.78)	1.10 (0.68–1.63)		

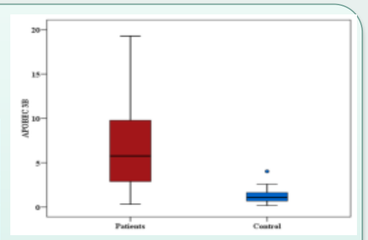

Figure 1: Box plot showing the expression of APOBEC3B in both MM patients and control groups.

Table 2: Relation between APOBEC3B expression levels (high-low) according to cutoff point of median and overall survival in pateints group (n = 50)

	Total No.	No. of Events	Mean (month)	Median (month)	% End of study	Log rank χ^2	Log rank p
APOBEC3B							
Low	25	3	11.920	–	88.0%	7.391*	0.007*
High	25	11	9.560	–	56.0%		

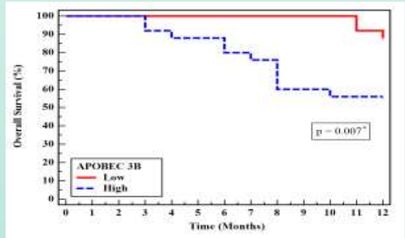

Figure 2:
Kaplan-Meier survival curve for Overall survival with APOBEC3B.

Table 3: Relation between APOBEC3B expression levels and relapse free survival in Survival cases (n = 36)

	Total No.	No. of Events	Mean (month)	Median (month)	% End of study	Log rank χ^2	Log rank p
APOBEC 3B							
Low	22	5	11.273	–	77.3%	9.597*	0.002*
High	14	9	6.786	4.00	35.7%		

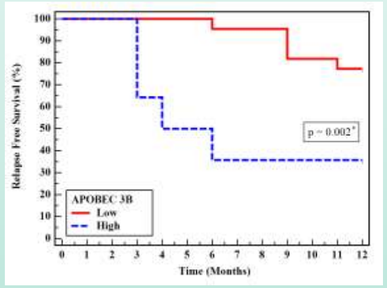

Figure 3:
Kaplan-Meier survival curve for Relapse Free survival with APOBEC 3B in Survival cases

Conclusion

- APOBEC3B is significantly over expressed in multiple myeloma (MM) patients and is strongly associated with poor clinical outcomes, including higher disease burden, renal impairment, and reduced overall and relapse-free survival, highlighting its role as a negative prognostic biomarker.
- Given its contribution to genomic instability and drug resistance, APOBEC3B represents a promising molecular target for future therapies, not only in MM but also across various malignancies where its over expression is linked to aggressive disease and poor prognosis.