Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2025.397585.4026 Volume 31, Issue 9 September. 2025
Manuscript ID ZUMJ-2506-4026
DOI 10.21608/ZUMJ.2025.397585.4026

ORIGINAL ARTICLE

Clinical Significance of Beclin 1 Expression in Patients of Acute Myeloid Leukemia

Amal A. Zidan[1], Fouad M. Abutaleb[2], Hana H. Elsaid[1], Mona M. Abdel-Wahab Sleem[1], Nahla I. Zidan[1]*

[1] Clinical Pathology Department, Faculty of Medicine, Zagazig university, Egypt
[2] Medical Oncology Department, Faculty of Medicine, Zagazig university, Egypt

Corresponding author:
Nahla Ibrahim Zidan
Email:
Nahlaiz@yahoo.com

Submit Date 04-07-2025
Revise Date 23-07-2025
Accept Date 04-08-2025

ABSTRACT

Background: Acute Myeloid Leukemia (AML) is an aggressive form of hematological malignancy in adults, marked by the buildup of immature white blood cells in the bone marrow and blood. Beclin 1, which is an autophagy gene, may play a role in leukemia progression, but its clinical significance in AML remains unclear. The purpose of this study was to assess Beclin 1 expression level as a prognostic marker in AML patients.

Methods: A prospective case-control study was conducted on 80 participants at Zagazig University Hospitals, divided into (Patient Group): 40 adult AML patients and (Control Group): 40 healthy controls. Blood and bone marrow samples were collected before starting treatment, and Beclin 1 expression was measured using quantitative real-time PCR.

Results: A significant drop was found in Beclin 1 levels among AML patients compared to healthy individuals ($p < 0.001$). Patients were divided according to level of expression.Those with reduced expression had poorer treatment outcomes as only 30.8% of them achieved complete remission, compared to 85.7% with normal expression group ($p = 0.001$). Moreover, the one-year overall survival was significantly lower in the reduced expression group (34.6%) than in the normal group (85.7%), with a fivefold increased risk of death (HR = 5.43, $p = 0.002$).

Conclusions: Beclin 1 expression is decreased in AML. Low Beclin 1 is associated with lower rates of complete remission. It could be a significant marker in predicting response to treatment and disease progression, so it may be of a potential use as target molecule in therapy.

Keywords: Beclin 1, Autophagy, Acute Myeloid Leukemia, Survival.

INTRODUCTION

Acute myeloid leukemia (AML) is a hematological malignancy which exhibits significant genetic heterogeneity and involves a buildup of immature myeloid blasts that don't behave normally, AML blasts keep uncontrolled proliferation and fail to mature properly [1, 2]. While standard chemotherapy has made a big difference in treating AML, many patients still relapse or develop resistance, which is a growing challenge [3].

Autophagy is basically the cell's recycling system; it maintains balance and keeps cells alive under stress. When cells are under pressure, whether from lack of nutrients or chemotherapy, autophagy kicks in to help them survive [4]. It's also crucial for keeping hematopoietic stem cells in good shape, partly by keeping their mitochondria's activity in check [5]. We've known for a while that autophagy is important for keeping cells normal, but its role in cancer is kind of a two-edged sword. On one hand, it maintains genome stability; [6]. On the other hand, cancer cells can ramp up autophagy to support their

extra energy needs and they can even use it to dodge chemotherapy effects [7].

Genes like Beclin 1, which suppress tumors, have been identified as an autophagy gene [8]. In AML specifically, Beclin 1 levels vary quite a bit and can have downstream effects on autophagy [9]. Research shows AML blasts often have lower expression of autophagy-related genes, including Beclin 1 [7]. These cells also exhibit reduced autophagy activity, which is characterized by the accumulation of damaged mitochondria with the presence of high levels of reactive oxygen species (ROS) causing disruption of DNA that occurs in AML blasts. So, the presence of mitochondrial autophagy defect enhances the malignant transformation of hematopoietic progenitor cells, leading to the development of AML [10]. The study hypotheses was that alteration in expression of Beclin 1 is a risk factor for AML, and it has an impact on the prognosis. The purpose of this study was to evaluate clinical significance of Beclin 1 expression level as a predictor for prognosis in patients with acute myeloid leukemia.

METHODS

We carried out this prospective case-control study at the Clinical Pathology Department and the Medical Oncology Department, Faculty of Medicine, Zagazig University. The study was carried out over a period from December 2020 to December 2022.

The study involved a total of 80 adult participants, who were categorized into two groups. The patient group included 40 newly diagnosed patients with de novo AML, comprising 27 males and 13 females, aged between 18 and 72 years. Patient group was classified according to Beclin 1 expression into 2 subgroups, those with normal expression (No=14) and the other with reduced expression (No=26). This classification into normal and reduced Beclin 1expression was according to median expression of the control group as a cut-off. The control group consisted of 40 apparently healthy individuals, with 19 males and 21 females, aged 19 to 70 years. The control group was well-matched with the patient group regarding age and sex. Sample size was calculated using the OpenEpi program.

Inclusion criteria for the patient group required participants to be over 16 years old, newly diagnosed with AML (excluding the M3 subtype), and have not yet received induction therapy. Individuals were excluded if they refused to participate, were younger than 16 years old, had promyelocytic leukemia, had been previously treated for AML, had other malignancies or a history of myelodysplastic or myeloproliferative syndromes, or suffered from impaired renal, liver, or cardiac function.

Treatment plan:

AML patients followed a standard induction protocol known as the 3+7 regimen, consisting of continuous cytarabine infusion (100 mg/m²/day) for 7 days and doxorubicin (25 mg/m²/day) for the first 3 days. For patients older than 60 years, a lower intensity regimen involving low-dose chemotherapy or hypomethylating agents was given.

Response to therapy and survival outcomes

Complete remission (CR) is characterized by normal marrow as regard morphology with less than 5% blasts, and peripheral blood counts having more than 1×10^9/L neutrophils and more than 100×10^9/L platelets. Relapse is characterized by >5% blast cells in the BM aspirate. Overall survival (OS) was measured from the time of AML diagnosis to the time of death regardless of the cause. Disease free survival (DFS) is the time from first CR to relapse or death. Those who were lost, or didn't express the event, were considered as censored patients.

Patients follow-up:

Follow up of the patients included CBC and bone marrow aspiration after induction chemotherapy, on day 28, to assess the remission response. Then, all patients were assessed again once every 3 months through clinical examination and CBC. If there was any sign of a relapse by clinical or blood film examination, marrow aspiration and examination was done. Then, all patients were

followed up for a period of one year to evaluate both OS and DFS.

All patients included the study were subjected to the following: a complete medical history, including age, sex, clinical manifestations like fever, fatigue, bone pain, bleeding, or hepatosplenomegaly, and any previous treatments. Physical examination done and focused on signs such as bleeding (purpura, ecchymosis), fever, gum hypertrophy, lymphadenopathy and organ enlargement. Laboratory investigations, included CBC, that was performed on automated counter (Sysmex XN2000, Japan), serum lactate dehydrogenase (LDH) was done on the Cobas 6000 autoanalyzer (Roche diagnostics, Germany), and erythrocyte sedimentation rate (ESR) recorded using VISION-B (YHLO Biotech, China). Bone marrow aspiration and cytological examination were done using Leishman and cytochemical stains. In addition, flow cytometry for immunophenotyping analysis was done on Becton Dickenson FACS Canto2 device (BD company, USA) to detect the following markers: CD33, CD13, MPO, HLADR, TDT, CD34 CD64, CD14, CD20, CD22 and CD3; finally, conventional cytogenetic analysis by G banding technique; and karyotyping according to International System for Human Chromosomes Nomenclature. 20 metaphases were examined for each patient to be evaluated and classified [11].

Molecular Detection of Beclin-1 Expression.

I. RNA Extraction and cDNA synthesis from Whole Blood

Total RNA was extracted from EDTA-anticoagulated whole blood using Genomic Total RNA Purification Kit (Jena Bioscience, Germany) and transcribed into cDNA using High-capacity cDNA Reverse Transcription Kit (Jena Bioscience, Germany) for RNA reverse transcription according to the manufacture's protocol, on a PCR thermal cycler (Veriti, Applied Biosystems, Japan). The resulting cDNA was used for subsequent qPCR.

II. Quantitative Real-Time PCR (qRT-PCR)

Gene expression analysis of Beclin 1 was carried out by quantitative real-time PCR using SYBR Green gene expression assay (Jena Bioscience, Germany). Real-time PCR reaction was run on the QuantStudio 5 system (ThermoFisher, Singapore). A house keeping reference gene GAPDH was used as an internal control for calibration. Primers were supplied by (Jena Bioscience, Germany) and had the following sequence; Beclin 1 primers sequence: Forward: 5'- CCAGGAACTCACAGCTCCATT-3', Reverse: 5'-ATGAATCTGCGAGAGACACCA-3'. GADPH primers sequence: Forward: 5'-TGGGTGGAATCATATTGGAAC3', Reverse: 5'-TCAACGGATTTGGTCGTATTG-3'. PCR reaction was carried out as follows: initial denaturation at 95 °C for 15 minutes then 45 cycles of denaturation at 95 °C for 10 seconds, annealing at 60 °C for 15 seconds, extension at 72 °C for 20 seconds, then Melting curve analysis for 15 seconds.

III. Data Analysis

Relative quantification of Beclin 1 mRNA expression levels was calculated using the comparative CT (ΔΔCT) method. The cycle threshold values were obtained for Beclin 1 and then normalized to GAPDH. Finally, Fold changes were calculated by the 2^−ΔΔCT [12].

Ethical approval

An approval from the institutional review board (ZU-IRB#5661/15-10-2019) was obtained. Then, an informed written consent was provided for each participant in the study before inclusion. Human subjects' research adhered to the guidelines set by the Declaration of Helsinki, as part of the World Medical Association's Code of Ethics.

Statistical analysis

Data were analyzed using SPSS v27. Qualitative variables were presented as frequencies (%) and compared using the Chi-square test. Quantitative data were expressed as mean ± SD or median, with comparisons made using the independent t-test or Mann–Whitney U test as appropriate. The receiver operating characteristic curve (ROC) curve analysis identified optimal cut-offs; area under the curve (AUC) classified diagnostic accuracy. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated. Significance was set

at $p < 0.05$. Kaplan–Meier curves with log-rank tests compared survival, and hazard ratios with 95% CI quantified risk between groups.

RESULTS

Beclin 1 expression levels and laboratory characteristics of patients at diagnosis:

The expression level of Beclin 1 in AML patients group was statistically significantly lower than the control group with median value of (0.25 vs 1; respectively) P<0.001 (Table 1).

The cut off value below which the sample should be considered as Beclin 1 reduced expression was determined using the median value of the control group (1 unit). Then, our patients were divided into Beclin 1 normal expression and reduced expression groups by using this cut off value (Table 1).

At diagnosis, 14 (35%) out of 40 newly diagnosed AML patients had normal Beclin 1 expression. While, 26 (65%) of patients had reduced expression. All control group subjects had normal Beclin 1 expression.

Regarding clinical and laboratory characteristics of the patients, reduced Beclin 1 expression group had significantly higher TLC, PB blasts and BM blasts than the normal expression group (P<0.001, 0.04 and 0.04; respectively), suggesting its correlation with disease severity (Table 4). While, no statistically significant differences were detected between both groups as regards clinical findings, age, sex, HB, platelets and LDH (Table 2)

Beclin 1 expression showed non-significant heterogeneity among FAB subtypes of AML between both normal and reduced expression groups (p=0.38), M2 subtype was the most frequent in both groups (42.9% vs 42.3%; respecrively). While, there was a statistically significant heterogeneity of Beclin 1 expression regarding cytogenetic risk stratification of patients being either favorable, intermediate or adverse risk (P=0.03). Favorable risk cytogenetics was more frequent among normal expression than reduced expression group (35.8%, 3.8%; respectively, P=0.44). While, intermediate and adverse risk were higher in the reduced expression than normal expression group (88.5% vs 57.1% and 7.7% vs 7.1% respectively), but with no statistically significant difference (P= 0.69, 0.22; respectively) (Table 2).

Prognostic significance of Beclin 1 low expression:

We studied the role of Beclin 1 reduced expression in predicting the treatment outcome of AML patients. Reduced Beclin 1 expression was significantly associated with poorer outcomes. Patients with reduced Beclin 1 expression had statistically significantly lower complete remission rates after induction than the normal expression group (30.8% vs. 85.7%, P = 0.001) (Table 3).

By applying ROC curve to detect the optimal cut off value which could predict complete remission response among the patients, At cut off >0.35, the sensitivity of Beclin 1 was 70%, specificity was 85%, PPV was 82.3%, NPV was 73.9% and accuracy was 77.5% in predicting the complete remission rate of the patients (Table 4 and Figure 1).

We applied Kaplan-meier survival analysis to investigate survival rates including both OS and DFS. Beclin 1 reduced expression group had a statistically significantly lower one-year OS than the normal expression group (one years median OS periods were 9.62 vs. 11.93 months with OS percent probability of 34.6% vs. 85.7%; respectively, HR = 5.43 and P =0.002). Also, reduced expression group show higher relapse and lower DFS rates than the normal expression group, but with no statistically significant differences (P> 0.05) (Table 3 and figure 2).

Table (1): Level of Beclin 1 expression among the studied AML patients and control groups

Variable	Patients (*n*=40)	Control (n=40)	P
Beclin-1 *Median* *Range*	 0.25 0.06-1.09	 1 0.85-1.07	 **<0.001****

****: Highly Significant (p<0.001)**

Table (2): Comparison between normal and reduced Beclin 1 expression in patient groups as regards demographic, clinical, and laboratory data

Variable	Beclin 1 expression		P
	Normal (*n*=14)	Reduced (n=26)	
Age (years) *Mean ± SD*	 47.36±14.82	 46.85±13.92	 0.91 NS
Sex*:* No. (%) *Female* *Male*	 6 (42.9) 8 (57.1)	 7 (26.9) 19(73.1)	 0.31 NS
Hepatomegaly No. (%)	2 (14.3)	10 (38.5)	0.11 NS
Splenomegaly No. (%)	4 (28.6)	14 (53.8)	0.13 NS
Lymphadenopathy No. (%)	0 (0)	2 (7.7)	0.29 NS
Purpura No. (%)	11 (78.6)	21 (80.8)	0.87 NS
Fatigue No. (%)	12 (85.7)	23 (88.5)	0.80 NS
Gum hypertrophy No. (%)	3 (21.4)	9 (34.6)	0.39 NS
Fever No. (%)	11 (78.6)	22 (84.6)	0.63 NS
TLC (x10^9/L) **Median** **Range**	 16.05 (2.4-157)	 62.95 (2.4-361)	 **<0.001****
HB (gm/dl) *Mean ± SD*	 8.39±1.26	 8.25±1.94	 0.80 NS
PLT (x10^9/L) *Median (Range)*	 43.5(10-108)	 49 (7-176)	 0.76 NS
PB blast (%) *Median (Range)*	 44.5(5-64)	 63.5(5-90)	 **0.04***
BM blast (%) *Mean ± SD*	 60.36±18.78	 70.62±21.64	 **0.04***
ESR (mm/hr) *Mean ± SD*	 74.43±23.84	 89.19±24.8 8	 0.07 NS
LDH (U/L) *Mean ± SD*	 513.5(138-914)	 615(216-950)	 0.19 NS
FAB subtypes: No. (%) M0 M1 M2 M4	 0 (0) 1 (7.1) 6 (42.9) 3 (21.4)	 3 (11.5) 5 (19.2) 11 (42.3) 4 (15.4)	 0.38 NS

Variable	Beclin 1 expression		P
	Normal (*n*=14)	Reduced (n=26)	
M5	4 (28.6)	3 (11.5)	
Cytogenetic: No. (%) *Normal* *Abnormal*	 8 (57.1) 6 (42.9)	 21 (80.8) 5 (19.2)	 0.11 NS
Cytogenic prognosis: No. (%) ***Favorable*** t(8;21) Inv (16) ***Intermediate*** Normal Del Y Tri 8 ***Adverse*** Monosomy 7 t(11,12) t(6,11)	 **5 (35.8)** 3 (60) 2 (40) **8 (57.1)** 8 (100) 0 (0) 0 (0) **1 (7.1)** 0 (0) 1 (100) 0 (0)	 **1 (3.8)** 1 (100) 0 (0) **23 (88.5)** 21 (91.3) 1(4.3) 1 (4.3) **2 (7.7)** 1 (50) 0 (0) 1 (50)	**0.03 *** 0.44 NS 0.69 NS 0.22 NS

SD: Standard deviation NS: Non significant (P>0.05) *:Significant (P<0.05)

****: Highly Significant (p<0.001)** **TLC: total leukocytic count HB: hemoglobin PLT:platelet**
PB: peripheral blood BM: bone marrow ESR: erythrocytw sedimentation rate LDH:lactate dehydrogenase

Table (3): Relation between normal and reduced Beclin-1 expression groups as regard response to induction therapy, follow up, one-year DFS, and overall survival

Variable	Beclin-1 expression		P
	Normal (*n*=14)	Reduced (n=26)	
Treatment response: No. (%) **CR**	 12 (85.7)	 8 (30.8)	 **0.001***
Relapse: No. (%)	1 (7.1)	3 (11.5)	0.11 NS
One year OS: Median (months) (CI 95%) *Percent probability* *Hazard ratio*	 11.93 (11.74-12.12) 85.7% 5.43 (1.39-21.2)	 9.62 (8.48-10.75) 34.6%	**0.002***
One year DFS: Median (months) (CI 95%) *Percent probability*	 11.5 (10.57-12.43) 90.4 %	 10.8 (8.86-12.74) 71.6%	**0.29** NS

NS: Non significant (P>0.05), *: Significant (P<0.05),

OS: Overall survival, DFS: disease free survival CR: complete remission

Table (4): Validity of Beclin-1 in prediction of CR among the studied patient group

Variable	*Cut off*	AUC (CI 95%)	Sensitivity	Specificity	PPV	NPV	Accuracy	p
Beclin-1	*>0.35*	0.80 (0.66-0.94)	70%	85%	82.3%	73.9%	77.5%	**0.001***

AUC: Area under curve, CI: Confidence interval, PPV: +ve predicted value, NPV: -ve predicted value, *: Significant (P<0.05)

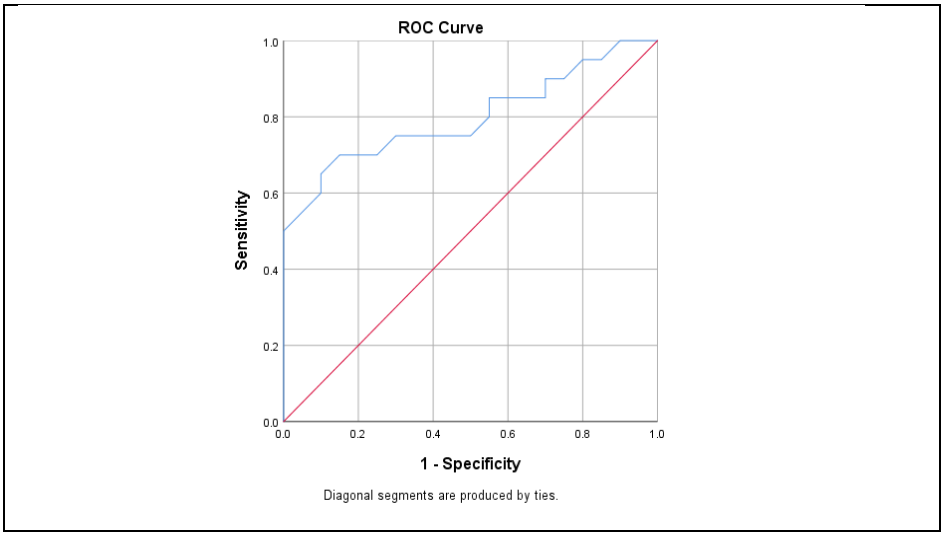
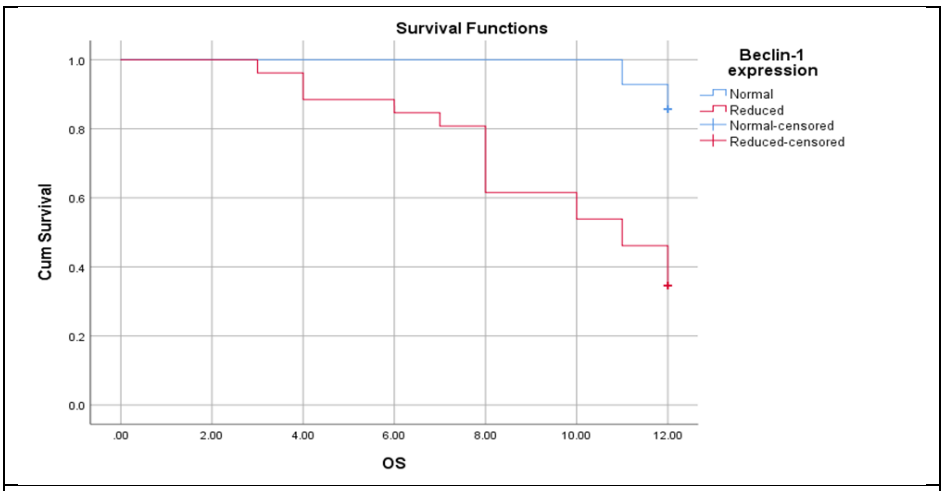
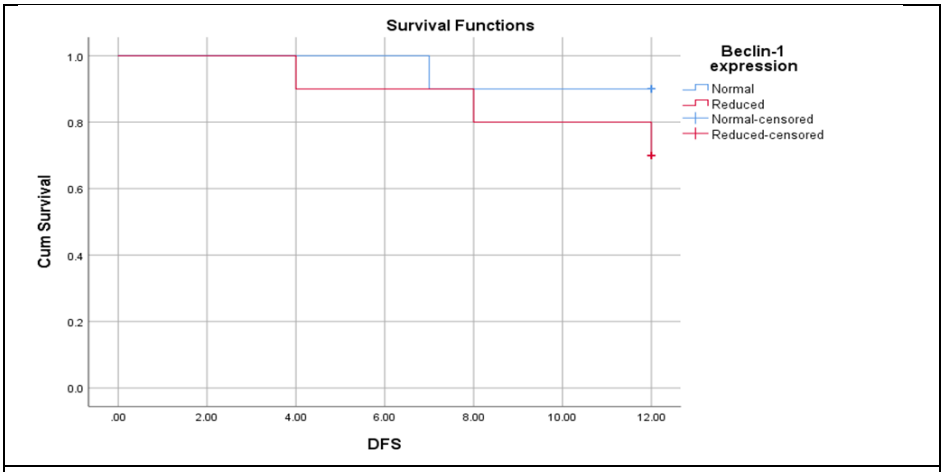


Figure 1: Roc curve for validity of Beclin-1 in prediction of CR among the studied patient group.



(A)



(B)

Figure 2: (A): Kaplan Meier curve for OS for normal and reduced Beclin-1 expression groups. (B): Kaplan Meier curve for DFS for normal and reduced Beclin-1 expression groups.

DISCUSSION

Beclin-1 plays a complex role in cancer biology, particularly in autophagy regulation. Its expression varies across different cancer types, including leukemia, influencing several cellular pathways [13]. In acute myeloid leukemia, blasts often exhibit reduced expression of autophagy related genes like Beclin 1, with decreased autophagic flux, and elevated ROS levels, which may contribute to disease progression [14].

In our study, the incidence of Beclin 1 reduced expression was 65% of AML patients, which is in line with study of Ghozlan **et al. [15]** (72%), but it was more than that reported by Zare-**Abdollahi et al**. **[13]** (45%). These results support the previous research as Beclin 1 could serve a tumor-suppressive function through mechanisms such as limiting DNA damage and preserving genomic integrity, thereby inhibiting malignant transformation [16]. In contrast to our result, **Tandel et al. [17]** showed that most of AML patients had increased Beclin 1 expression (76%). These differences between studies may be due to the use of different reference genes in evaluating the expression level of Beclin 1 gene, population differences, sample heterogeneity, or variations of AML subtypes. These conflicting reports highlight the need for broader, standardized investigations into Beclin 1's role in AML pathogenesis, **Lian et al. [18]** emphasized the dual nature of autophagy in cancer it can be both protective and harmful depending on the cellular context and tumor environment.

Regarding the association between Beclin 1 gene expression and demographic data of AML patients, in the current study, the mean value of the age of the normal and reduced Beclin 1 gene expression groups was 47.36±14.82 and 46.85±13.92 years; respectively with no statistically significant difference observed between both groups as regards age. These results are supported by similar observations from **Lian et al. [18]** as regards age with median value of (50.5 vs 60 years, p=0.382). However, in contrast, both **Zare-Abdollahi et al. [13]** and **Ghozlan et al. [15]** who found that the lower Beclin 1 expression was more frequently presented among older individuals (P<0.001).

Also, in this study, no statistically significant difference was detected between the group with reduced Beclin 1 expression compared to that group with normal expression of Beclin 1 as regards sex, which was in agreement with other studies [13,15,17].

Evaluation of the hematological characteristics of the patients in this study demonstrated that reduced Beclin 1 gene expression group had a statistically significant higher TLC and BM blasts when compared to that group with normal expression. These

findings agreed with previous reports showing high WBC counts in patients with low Beclin 1 expression [13,15]. The inverse correlation may reflect disrupted autophagy's effect on unchecked cell proliferation and survival, as Beclin 1 is known to interface with apoptotic pathways, including ATG7 [13,19]. In contrast, **Tandel et al. [17]** reported a positive correlation, higher Beclin 1 linked with increased WBC counts (r=0.697; P<0.0001) suggesting that autophagy might also promote leukemic cell growth in certain contexts. In addition, Hemoglobin levels and platelet counts showed non-significant difference between both groups (P=0.08 and 0.76; respectively).

We didn't find a significant link between Beclin 1 expression and FAB subtype, which supports findings by **Ghozlan et al. [15] and Folkerts et al. [20]**, who reported that reduced expression was more frequent in M1 and M2, yet this association didn't reach a significant level (P=0.105).

In the current study regarding cytogenetic risk, patients with reduced Beclin 1 expression was found most frequently in patients with intermediate-risk kayrotype (88.5%) (P=0.03), particularly among those with normal karyotypes (91.3%). While, in that group with normal Beclin 1 expression; Favorable cytogenetic was more frequent compared to that group with reduced expression (35.8% and 3.8%; respectively). **Ghozlan et al. [15]** similarly observed lower Beclin 1 expression in those with intermediate and adverse karyotypes compared to both favorable risk and control groups.

Response to induction chemotherapy is a major prognostic indicator in AML. After induction chemotherapy, to assess the impact of Beclin 1 expression on the outcome, it was found that CR rate was statistically significantly lower in the reduced expression group than that in the normal expression group (30.8% vs 85.7%; respectively). This was in agreement with **Ghozlan et al. [15]** who showed that non-responders had significantly reduced Beclin 1 expression (P=0.002), and **Marconi et al. [21]** linked reduced autophagy gene expression including Beclin 1 to therapy resistance (P<0.001)

In contrast, **Tandel et al. [17]** reported that patients achieving complete remission had lower Beclin 1 levels compared to newly diagnosed cases (P=0.004), suggesting autophagy may be upregulated during therapy as a resistance mechanism. **Lian et al. [18]** also found a non-significant association between decreased Beclin 1 and higher remission rates, further supporting autophagy's ambiguous role. Such inconsistencies likely reflect differences in methodology, population characteristics, disease subtypes, or gene expression assays. Further standardized research is needed to clarify Beclin 1's role as a biomarker.

Some studies have explored how Beclin 1 may interact with key mutations in AML. **Watson et al. [10]** noted that survival pathway of AML cells that is mediated by FLT3-ITD mutations, which protect AML cells from apoptosis via STAT5 activation and upregulation of MCL1, could be intersected by Beclin 1, suggesting potential for targeted therapies in genetically defined subtypes [13].

Differences in findings among various studies likely reflect methodological variations such as differences in AML classification, gene detection techniques, and analytical tools. Patients demographics and disease heterogeneity may also influence outcomes and gene expression profiles [22].

In this study, the cut off value of Beclin 1 expression level for prediction of achievement of complete remission was determined by applying The ROC curve. The optimal cut off value was >0.35 with AUC of 0.80, sensitivity of 70% and specificity of 85%, indicating that reduced expression confers a poor outcome with resistance to therapy. The results of this study reported that Beclin 1 can be an excellent biomarker for the assessment of complete remission response of AML patients [23].

This finding is in line with **Wang et al. [24]**, who reported an AUC of 0.826 for Beclin 1 in predicting AML progression. In high-risk

patients, the AUC dropped slightly to 0.675, still indicating moderate predictive power.

Regarding relapse, in the current study, four patients who initially achieved complete remission eventually relapsed. However, relapse rates did not differ significantly between the reduced and normal Beclin 1 expression groups (P=0.11). These findings are in line with those of **Zare-Abdollahi et al. [13]** and **Liang et al. [26]**, who found no clear link between Beclin 1 expression levels and relapse incidence.

Notably, patients with reduced Beclin 1 expression had a significantly shorter OS than those with normal expression [9.6 vs. 11.9 months; HR = 5.43; P = 0.002], suggesting potential prognostic value. However, DFS did not differ significantly between both groups (10.8 vs. 11.5 months; P = 0.29).

This finding regarding OS was also reported by **Wang et al. [24]** and **Radwan et al. [25]**, who found that low Beclin 1 expression correlated with poorer survival outcomes. **Wang et al. [24]** also proposed that miR-17-5p overexpression may contribute to Beclin 1 suppression and cancer progression in AML via impaired autophagy regulation.

While **Liang et al. [26]** reported no impact of Beclin 1 expression on OS overall, they did find worse OS within the unfavorable-risk subgroup when expression was low (P = 0.029). On the other hand, **Lian et al. [18]** observed that higher Beclin 1 expression was linked to shorter OS (P = 0.02), potentially due to differences in patient age, treatment regimens, and leukemia subtypes.

In addition, regarding DFS, our results are in line with **Liang et al. [26]** who also found no significant link between Beclin 1 and disease-free survival [18]. However, other studies such as **Radwan et al. [25]** and **Wang et al. [24]** reported significantly shorter DFS in AML patients with reduced Beclin 1 expression, highlighting the variability of outcomes depending on study parameters.

This study has a few limitations, such as the sample size was small and collected from one institution, which may limit the generalization of the results. Also, Beclin 1 expression was assessed only at diagnosis, and dynamic changes during or after treatment were not evaluated. The follow-up duration was limited to one year, which may be insufficient to fully assess long-term survival outcomes and relapse rates. Additionally, molecular subtyping beyond cytogenetics, such as FLT3, NPM1, or IDH mutations, was not included, which could further clarify Beclin 1's prognostic role in specific AML subgroups.

Conclusion

Beclin 1 gene expression is decreased in AML patients. Low Beclin 1 could be associated with lower rates of CR and significantly shorter OS. It could be a specific significant marker for predicting response to treatment and disease progression, so it may be of a potential use as target molecules in therapy.

Conflict of interest: None

Financial disclosures: None.

REFERENCES

1-Marcucci G, Mrózek K, Ruppert AS, et al. Abnormal cytogenetics at date of morphologic complete remission predicts short overall and disease-free survival, and higher relapse rate in adult acute myeloid leukemia: results from Cancer and Leukemia Group B STUDY 8461. J Clin Oncol. 2004;22(12):2410–18.

2- Beaton M, Peterson GJ, O'Brien K. Acute myeloid leukemia: advanced practice management from presentation to cure. J Adv Pract Oncol. 2020;11(8):836–43.

3-Ebinama U, George B. Revolutionizing acute myeloid leukemia treatment: a systematic review of immune-based therapies. Discover Oncol. 2025;16(1):89–96.

4- Tanida I. Autophagosome formation and molecular mechanism of autophagy. Antioxid Redox Signal. 2011;14:2201–11.

5-Ho TT, et al. Autophagy maintains the metabolism and function of young and old stem cells. Nature. 2017;543:205–11.

6- Singh SS, Vats S, Chia AY, Tan TZ, Deng S, Ong MS, et al. Dual role of autophagy in hallmarks of cancer. 2017;37:1142–58.

7- Fulda S. Autophagy in cancer therapy. Front Oncol. 2017;7:128–41.

8-Galluzzi L, Baehrecke EH, Ballabio A, et al. Molecular definitions of autophagy and related processes. EMBO J. 2017;36:1811–36.
9- Baquero P, Dawson A, Mukhopadhyay A, Kuntz EM, Mitchell R, Olivares O, et al. Targeting quiescent leukemic stem cells using second generation autophagy inhibitors. Leukemia. 2018:451–58.
10- Watson AS, Riffelmacher T, Stranks A, Williams O, De Boer J, Cain K, et al. Autophagy limits proliferation and glycolytic metabolism in acute myeloid leukemia. Cell Death Discov. 2015;1:1–10.
11- Swansbury J. Cancer cytogenetics: methods and protocols; cytogenetic techniques for myeloid disorders. Mol Biol 2003; 220:43–57.
12- Livak K, Schmittgen T. Analysis of relative gene expression data using real time quantitative PCR and the 2(-Delta Delta C(T)) method. Methods. 2001; 25:402–8.
13- Zare-Abdollahi D, Safari S, Movafagh A, Ghadiani M, Tabarraee M, Riazi-Isfahani S, et al. Expression analysis of BECN1 in acute myeloid leukemia: association with distinct cytogenetic and molecular abnormalities. Int J Lab Hem. 2015;38:125–32.
14- Keyvan L, Bidoki SK, Zare Abdollahi D, Mansouri N, et al. Lack of altered BECN1 gene expression in Iranian patients with acute myeloid leukemia. Asian Pac J Cancer Prev. 2016;17:5173–77.
15-Ghozlan M, Farweez B, Safwat N, Hassan N, Elsalakawy WA. Reductive regulation of BECN1 gene in adult Egyptian patients with de novo AML. Egypt J Med Hum Genet. 2020;21:45–53.
16-Jing Y, Zhang J, Zhu Y, Wang L, et al. Targeting autophagy and beyond: deconvoluting the complexity of Beclin1 from biological function to cancer therapy. Acta Pharm Sin B. 2023;13:4688–714.
17-Tandel P, Ebrahimi E, Ramzi M, Rezvani A, Ranjbaran R, et al. Evaluation of BECN1 gene expression in remission-induction therapy of acute myeloid leukemia. Shiraz E-Med J. 2020; 21: e96683.
18.Lian Y, Xie Y, Hong M, Zhu Y, Zhao H, et al. Clinical significance of BECLIN1 and ATG5 expression in acute myeloid leukemia patients. Int J Clin Exp Pathol. 2018;11:1529–37.
19-Vinod V, Padmakrishnan CJ, Vijayan B, et al. 'How can I halt thee?' The puzzles involved in autophagic inhibition. Pharmacol Res. 2014;82:1–8.
20-Folkerts H, Hilgendorf S, Wierenga A, Jaques J, et al. Inhibition of autophagy as a treatment strategy for p53 wild-type acute myeloid leukemia. Cell Death Dis. 2017; 8:e2927.
21-Marconi G, Fontana M, Papayannidis C, Padella A, Monaco S, Abbenante M, et al. Prognostic significance of alterations of pathways regulating autophagy in acute myeloid leukemia. J Clin Oncol. 2017;35:7038–51.
22- Döhner H, Estey E, Grimwade D, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood. 2017; 129: 424–47.
23-Gajjar A, Ribeiro R, Hancock M, et al. Persistence of circulating blasts after 1 week of multiagent chemotherapy confers a poor prognosis in childhood acute lymphoblastic leukemia. Blood. 1995;86:1292–95.
24-Wang W, Liu J, Chen K, Wang J, Dong Q, Xie J, et al. Vitamin D promotes autophagy in AML cells by inhibiting miR-17-5p induced Beclin-1 overexpression. Mol Cell Biochem. 2021;476:3951–62.
25-Radwan S, Hamdy N, Hegab H, et al. Beclin-1 and hypoxia-inducible factor-1α gene expression: potential biomarkers in acute leukemia patients. Cancer Biomark. 2016;16:619–26.
26- Liang P.Q., Miao M., Liu Z.G., Hu R., Jiang H.N., Li C., et al. (2018):Expression of autophagy genes in acute myeloid leukemia: associations with clinical characteristics and prognosis. Neoplasma. ;65:807–14.

Citation

Zidan, A., Abutaleb, F., El-said, H., Abdel-Wahab, M., Zidan, N. Clinical Significance of Beclin 1 Expression in Patients of Acute Myeloid Leukemia. ***Zagazig University Medical Journal*****, 2025; (4736-4746): -. doi: 10.21608/zumj.2025.397585.4026**