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Aberrant CD7 antigen expression as a prognostic factor for remission achievement in adult *de novo* acute myeloid leukemia patients treated with 3 + 7 regimen

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Abstract:

BACKGROUND: Aberrant expression of cluster of differentiation 7 (CD7) antigen has emerged as a potential prognostic factor in adult *de novo* acute myeloid leukemia (AML) patients treated with the 3 + 7 regimen. Understanding the significance of CD7 expression in predicting remission achievement and treatment outcomes is crucial for developing personalized therapeutic strategies in AML.

OBJECTIVES: The objectives of this study were to investigate the prognostic impact of CD7 antigen expression on remission achievement and overall survival (OS) in adult *de novo* AML patients receiving the 3 + 7 chemotherapy regimen.

MATERIALS AND METHODS: This study included 37 adult *de novo* AML patients treated with the standard 3 + 7 induction regimen (3 days of daunorubicin plus 7 days of cytarabine). CD7 antigen expression was evaluated using multicolor flow cytometry. Patients were categorized into CD7-positive and CD7-negative groups. Clinical and laboratory parameters, including remission status at day 28 and OS duration, were collected and statistically analyzed to determine the association between CD7 expression and treatment outcomes.

RESULTS: CD7 positivity was significantly associated with lower remission rates, with only 27.8% of CD7-positive patients achieving complete remission, compared to 68.4% of CD7-negative patients (P = 0.01). In addition, CD7-positive patients had a significantly shorter mean OS of 2.6 months, whereas CD7-negative patients had a mean survival of 4.6 months (P = 0.03).

CONCLUSION: CD7 antigen expression in *de novo* AML is significantly associated with reduced remission rates and shorter survival, suggesting its potential role as a prognostic biomarker. Assessing CD7 expression at diagnosis may help stratify patients and guide individualized therapeutic strategies in AML.

Keywords:

Acute myeloid leukemia, cluster of differentiation 7 antigen, prognostic marker, remission achievement

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Introduction

Acute myeloid leukemia (AML) is a heterogeneous and aggressive hematologic malignancy characterized by the clonal expansion and accumulation of immature myeloid progenitor cells in the bone marrow (BM) and peripheral blood (PB), leading to BM failure and impaired hematopoiesis.[1,2] The standard induction therapy for AML, commonly referred to as the 3 + 7 regimen, involves the administration of cytarabine (Ara-C) for 7 days in combination with an anthracycline, such as daunorubicin

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or idarubicin, for 3 days. This regimen is designed to achieve complete remission (CR) by eradicating leukemic blasts. Despite its widespread use, clinical responses to the 3 + 7 regimen vary significantly among patients, highlighting the necessity of identifying predictive markers that can inform prognosis and therapeutic decisions.[3,4]

Although treatment advances have improved remission rates in some AML subgroups, the prognosis for adult patients with *de novo* AML remains inconsistent and often poor. This variability emphasizes the urgent need for reliable prognostic biomarkers to guide risk-adapted therapy and improve clinical outcomes.

One such biomarker of growing interest is the aberrant expression of cluster of differentiation 7 (CD7), a transmembrane glycoprotein typically expressed on T cells, natural killer (NK) cells, and a subset of hematopoietic progenitors.[5] In AML, CD7 expression on myeloid blasts is considered atypical, as these cells do not normally express lymphoid-associated markers.[6] The prevalence of CD7 expression in AML varies widely, ranging from 10% to 30% depending on the population studied and the immunophenotypic criteria employed.[7-9]

The presence of CD7 on leukemic blasts has also attracted attention as a potential target for novel therapies. Experimental approaches have explored the use of CD7-directed monoclonal antibodies, antibody-drug conjugates, and chimeric antigen receptor T-cell therapies. However, the clinical translation of these modalities is still limited by challenges such as antigen heterogeneity and the potential for on-target, off-tumor effects due to CD7 expression on normal immune cells.[10-12]

Given these considerations, the current study aims to investigate the clinical significance of aberrant CD7 antigen expression as a prognostic factor in adult *de novo* AML patients treated with the standard 3 + 7 regimen. By examining the correlation between CD7 expression status and remission achievement, this study seeks to contribute to the development of improved risk stratification tools and support the implementation of personalized treatment strategies in AML management.

Materials and Methods

This study is a retrospective observational analysis conducted on patients diagnosed with *de novo* AML. A total of 37 adult Iraqi patients were included, all of whom were newly diagnosed and referred to the Hematology and BM Transplantation Center at the Medical City Complex in Baghdad, Iraq, during the period from October 2022 to April 2023. The inclusion criteria required the availability of complete diagnostic profiles, including multicolor flow cytometric immunophenotyping results.

The provisional diagnosis of AML was established by a consultant hematopathologist based on findings from bone marrow aspirate (BMA) and/or PB smear examinations. Flow cytometric immunophenotyping was performed using the BD FACS-Canto II System (Becton Dickinson, USA), employing a standardized leukemia panel of fluorochrome-conjugated monoclonal antibodies. Raw data were retrieved from the flow cytometry (FCM) center in electronic format.

Patients' responses to induction therapy (typically the "3 + 7" regimen) were clinically evaluated and documented on day 28 post-treatment initiation. Clinical and laboratory parameters – including hemoglobin (HGB), white blood cell (WBC) count, platelet (PLT) count, and blast percentage in PB and BM – were recorded at diagnosis. Overall survival (OS) was tracked for up to 180 days.

For comparative analysis, 20 healthy control individuals, matched for age and sex and with no history of hematological or chronic illness, were recruited. They exhibited normal hematological parameters and were not undergoing any medical treatment at the time of enrollment.

The control group was included to establish a quantitative baseline for hematological parameters and to statistically illustrate the degree of deviation observed in AML patients.

This research was approved by the Research Ethics Committee at the College of Science, University of Baghdad, under approval number CSEC/0922/0082, dated September 22, 2022. All data were anonymized to ensure patient confidentiality.

Patients' inclusion criteria

- Patients were randomly selected based on sex
- All AML patients were required to be 14 years old or older
- All patients were newly diagnosed with *de novo* AML and had not received any prior chemotherapy before blood sample collection
- Patients with AML were typically diagnosed through cytomorphology and FCM.

Exclusion criteria

- Patients younger than 14 years and over 60 years
- Individuals with acute promyelocytic leukemia and mixed lineages AL
- Patients with AML featuring central nervous system infiltration or other extramedullary manifestations

- Secondary AML including patients who had received prior treatment with hypomethylating agents for myelodysplastic syndrome and had progressed to AML
- Association with other malignancies.

Diagnosis and monitoring of acute myeloid leukemia patients

PB and BMA samples were collected from patients according to a specialized diagnostic protocol. This protocol included a complete blood count (CBC), evaluation of a blood film, and morphological examination of BMA smears to assess blast cells and myeloid differentiation. In addition, BMA samples underwent multicolor FCM testing to estimate the presence of markers such as CD7, CD11c, CD13, CD14, CD19, CD33, CD34, CD45, CD64, and an additional identifier. Patient information, including age, sex, and clinical presentation, was collected from medical records. Hematological parameters were measured using a Nihon Kohden Celltac F Automatic CBC Analyzer.

Therapy and follow-up

Patients received induction chemotherapy consisting of two drugs: daunorubicin and cytarabine, in accordance with the standard "3 + 7" regimen.

For all patients with AML, CBC and blood film were repeated at day 28 after completion of chemotherapy induction to check hematological parameters if recovery was occurred and BM smear was repeated to confirm remission. Patients were evaluated for CR achievement 3 weeks after one cycle of chemotherapy. CR was defined as (<5% BM blast cells of normal cellularity and restoration of normal PB values of at least 1500/μL neutrophils and 100,000/μL PLTs).

Statistical analysis

The statistical analysis of the results was conducted using GraphPad Prism 9 and Microsoft Office Excel software 2023. Statistical significance was determined using the Pearson Chi-square test and Student's-*t*-test. $P < 0.05$ was considered statistically significant.

Results

This study involved 37 patients diagnosed with AML, with ages ranging from 14 to 60 years. The mean age was 43.56 ± 12.97 years, and the standard error of the mean was 2.076 years. This broad age range reflects the variable onset of AML across age groups.

The gender distribution, as shown in Table 1, was nearly equal, with 49% male and 51% female patients, indicating no significant gender bias in disease occurrence. Regarding clinical presentation, the most common initial features were pallor (37%) and fever (20%), followed by lymphadenopathy (8%) and pancytopenia (8%). Other symptoms included fatigue, anemia, hepatosplenomegaly, ecchymosis, and flu-like symptoms.

Hematological findings revealed significant differences between AML patients and healthy controls. As detailed in Table 2, AML patients showed a significant decrease in hemoglobin, RBCs, and PLT counts, with a significant increase in WBCs. PB blasts were present only in AML patients (mean 45.4%), whereas BM blasts averaged 58.08%.

Flow cytometric analysis showed aberrant CD7 expression in 18 out of 37 patients (48.6%). Among CD7-negative patients, 68.4% achieved CR, whereas only 27.8% of CD7-positive patients responded to induction therapy. This difference was statistically significant ($P = 0.01$), as shown in Table 3.

Furthermore, OS analysis revealed that CD7-negative patients had a longer mean survival time of 4.6 months compared to 2.6 months in CD7-positive patients ($P = 0.03$), as shown in Table 4.

Table 1: Acute myeloid leukemia patients' categorization by sex and initial clinical features

	AML case (*n*=37), *n* (%)
Sex	
Male	18 (49)
Female	19 (51)
Initial clinical features	
Fatigue	2 (4)
Anemia	2 (4)
Infection	1 (2)
Fever	10 (20)
Hepatosplenomegaly	3 (6)
Lethargy	1 (2)
Lymphadenopathy	4 (8)
Pallor	18 (37)
Pancytopenia	4 (8)
Bone pain	1 (2)
Flu-like	1 (2)
Ecchymosis	2 (4)

AML=Acute myeloid leukemia

Table 2: Hematological results of all the studied group

Parameter, mean±SE	Control group (*n*=20)	AML patients (*n*=37)	*P*
Hb (g/dL)	12.84±0.66	8.576±0.3521	0.000*
RBCs ($\times 10^6$/μL)	5.2±0.16	2.88±0.127	0.000*
WBCs ($\times 10^3$/μL)	7.601±0.73	62.13±19.19	0.008*
Platelets ($\times 10^3$/μL)	221.5±12.79	42.95±5.69	0.000*
BM blasts (%)	-	58.08±4.7	
PB blasts (%)	0.0±0.0	45.4±4.2	0.000*

WBCs=White blood cells, AML=Acute myeloid leukemia, RBCs=Red blood cells, Hb=Hemoglobin, BM=Bone marrow, PB=Peripheral blood, SE=Standard error, *Significant = $P \leq 0.05$

Table 3: Relation of aberrant antigen expression to response to induction chemotherapy

Outcome	CD7−	CD7+	χ^2	*P*
CR from the first time	13	5	6.11	0.01*
No remission	6	13		
Total number of patients	19	18		

CD 7=Cluster of differentiation 7, CR=Complete remission, *Significant = $P \leq 0.05$

Table 4: Overall survival

Parameter	Mean overall survival (months)	χ^2	*P*
CD7 negative	4.6	4.500	0.03*
CD7 positive	2.6		

CD 7=Cluster of differentiation 7, *Significant = $P \leq 0.05$

Discussion

The broad age range and mean age of 43.56 years observed in this study align with findings from Iraq and some international studies, which indicate that AML commonly affects adults in the 40–60-year age group.[13-16] The nearly equal gender distribution further supports epidemiological data suggesting no significant gender bias in AML incidence.

Clinical manifestations such as pallor, fever, and hepatosplenomegaly are consistent with the known effects of BM failure and leukemic infiltration. Fatigue and anemia result from impaired erythropoiesis, whereas fever may signal infection or leukemic cell-driven cytokine release.[17-19] Hepatosplenomegaly indicates extramedullary hematopoiesis, and pallor reflects low hemoglobin levels.[20,21] Additional features such as lymphadenopathy, pancytopenia, and ecchymosis add to the typical clinical picture seen in AML.[22]

The hematological abnormalities observed – marked cytopenias and elevated WBC counts—are a consequence of malignant blast infiltration in the BM, leading to ineffective hematopoiesis. These findings are consistent with previous studies emphasizing their diagnostic and prognostic significance.[23,24]

A key result of this study was the impact of CD7 expression on treatment outcomes. Patients with CD7 expression had a significantly lower CR rate and shorter OS, highlighting CD7 as a marker of chemoresistance. These observations are supported by prior research linking CD7 positivity with poor prognosis and reduced treatment efficacy in AML.[25-27]

The study also showed that 30% of CD7-positive patients failed to respond to induction therapy, with two early deaths. This matches earlier reports indicating worse disease-free and OS among CD7-positive patients compared to CD7-negative individuals.[28-32]

Mechanistically, CD7 is a transmembrane glycoprotein normally found on T-cells and early hematopoietic progenitors. Its aberrant expression in AML suggests a less differentiated, more aggressive leukemic clone. CD7 has been associated with other high-risk mutations such as FLT3-ITD and contributes to chemotherapy treatment failure through the activation of PI3K/AKT and MAPK/ERK survival pathways.[33] It also disrupts immune surveillance, allowing leukemic cells to evade cytotoxic responses from T and NK cells.[34,35]

Conclusion

CD7 expression in *de novo* AML plays a significant role in determining the prognosis and treatment outcomes for patients. The aberrant expression of CD7 is associated with poor remission rates, shorter OS, and increased treatment failure, as CD7positive patients often exhibit reduced responsiveness to induction therapy.

Limitations

This study is limited by its relatively small sample size and retrospective design. In addition, the lack of comprehensive cytogenetic and molecular data restricts our ability to perform full risk stratification or explore interactions between CD7 expression and specific gene mutations such as *FLT3* or *NPM1*. Prospective studies with larger cohorts and broader molecular profiling are warranted to validate and expand upon these findings.

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Conflicts of interest

There are no conflicts of interest.

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