

Prognostic Significance of CD7 Expression in Acute Myeloid Leukemia.

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Abstract

Background: Expression of the T-cell lymphoid marker CD7 in acute myeloid leukemia (AML) is considered a poor prognostic factor. In 88% of AML cases, aberrant expression of phenotypic markers has been reported.

Objectives: To determine the frequency of aberrantly expressed CD7 in adult patients with AML and its effect on their response to induction therapy in AML subtypes.

Methods: This cross-sectional study included 50 adult patients diagnosed with de novo AML at Baghdad Teaching Hospital, Medical City Complex, from January to December 2019. Based on the French-American-British (FAB) criteria, the patients were divided into two groups: monocytic and non-monocytic. Flow cytometry was used to demonstrate CD7 expression in blasts in whole blood or bone marrow aspirate samples. Response to induction therapy was determined after 4–5 weeks. The chi-square test was used to explore associations between discrete variables.

Results: CD7 was expressed in 36% of AML patients, and 88.9% of these patients had incomplete remission. Thirty patients (60%) had non-monocytic AML subtypes, and 20 patients (40%) had M4 or M5 subtypes. A significant positive association between CD7 expression and poor response to remission induction was found. There was no statistically significant difference between CD7 expression and either monocytic or non-monocytic AML subtypes. Only 20 patients (40%) achieved complete remission (CR) after induction therapy. The other 30 patients (60%) had incomplete remission (IR).

Conclusions: CD7 is expressed in a substantial portion of AML patients. High levels of this lymphoid marker correlate with incomplete remission following induction therapy, which portending poor prognosis.

Keywords: Acute myeloid Leukemia; CD7 expression; Monocytic; Non-Monocytic; Response to induction remission.

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Introduction

Acute myeloid leukemia (AML) is a disease that looks different in terms of its morphology, immunophenotype, and cytogenetics. At diagnosis, $\geq 20\%$ myeloblasts in the bone marrow and/or blood are required. However, it can be identified with $< 20\%$ blasts if certain cytogenetic or molecular genetic abnormalities unique to leukemia are present (1). AML is the most common type of acute leukemia in adults. The average age is 65 years. It constitutes only a small proportion (10–15%) of childhood leukemia. According to the World Health Organization, AML is categorized by prognosis, which is largely determined by cytogenetic and molecular alterations, as well as the effectiveness of first-line treatment (2).

AML is classified according to the World Health Organization (WHO; 2022) scheme. Approximately 60% of AML cases exhibit karyotype abnormalities on cytogenetic analysis, and most cases with a normal karyotype carry mutations in genes such as *FLT3*, *NPM1*, *CEBPA*, or *DNMT3A*, which are detected only by molecular methods (2). Flow cytometry of bone marrow aspirates or peripheral blood is important for determining whether a patient has AML and the type of immune system linked to the disease (2). Prognosis is largely determined by cytogenetic and molecular alterations, as well as the effectiveness of first-line treatment.

The 3+7 regimen for AML treatment involves the administration of cytarabine for seven days and an anthracycline, such as daunorubicin or idarubicin, for three days. This aims to kill all leukemic blasts and achieve complete remission (CR). However, patients experience different responses to this treatment. This underscores the importance of finding a predictive marker to help diagnose and treat patients (3, 4). In AML patients, abnormal expression of lymphoid markers, such as CD2, CD3, CD5, CD7, CD10, and CD19, is a major independent risk factor that impacts how well they will respond to treatment (5). Some patients with AML express a T-cell lymphoid marker called CD7. This marker is associated with poor outcomes in myeloid malignancies (6). It is unusual for myeloid blasts to produce CD7, because these cells usually do not show lymphoid-associated markers (7). The research aimed to identify the impact of CD7 expression in de novo untreated AML patients, determine the response to induction therapy, and correlate its presence with different AML subtypes.

Patients and methods:

This cross-sectional study was conducted at the Baghdad Teaching Hospital, Medical City Complex, Baghdad, Iraq from January to December 2019. Fifty adults who had recently been diagnosed with AML were recruited for the study. Based on the FAB criteria, patients were divided into two groups: monocytic (M4 and M5) and non-monocytic (M0, M1,

M2, M6, and M7). All patients were treated with the standard "3+7" induction chemotherapy protocol. Patients were categorized into two groups: those who achieved CR and those who experienced partial remission/induction resistance (IR). (8) Flow cytometric examination of fresh peripheral blood or bone marrow samples from all patients to detect CD7 expression was performed using a BD FACS Canto II flow cytometer (Becton Dickinson Immune Cytometry Systems, San José, CA, USA). Forward and side scatter (SSC) strategies, along with CD45 intensity versus SSC dot plots, were applied to identify blast cells. CD7 was considered positive when $\geq 20\%$ of the blast cells expressed the antigen.

The markers used to isolate blast cells include CD34, CD117, CD33, CD13, CD15, CD11b, CD14, CD64, CD36, and CD11c.

Inclusion criteria were:

1. Newly diagnosed *de novo* AML patients.
2. Adult patients aged ≥ 15 and < 60 years.
3. Patients exclusively treated with the "3+7" protocol.

Exclusion Criteria:

1. Patients with a history of myelodysplastic syndrome or therapy-related secondary AML cases.
2. Patients with AML-M3 (different treatment protocol).

Research approval was granted by the Research Ethics Committees of the Medical City Health Directorate and the Department of Pathology and Forensic Medicine, College of Medicine, University of Baghdad. All participants provided informed consent.

Statistical analysis: Frequencies and percentages were used to show categorical statistics. The chi-square test was used to find the associations between variables. A P-value of < 0.5 was considered significant.

Results

Non-monocytic AML subtypes were found in 30 patients (60%), while 20 patients were in M4 and M5 subtypes (40%). After induction therapy, only 20 (40%) patients achieved CR, while 30 (60%) had IR. CD7 was expressed in only 18 cases (36%), as shown in **Table 1**.

Variables	No. (%)
AML Subtype	
Non-monocytic	30 (60%)
Monocytic	20 (40%)
Response to treatment	
Incomplete remission (IR)	30 (60%)
Complete remission (CR)	20 (40%)
CD7 Expression	
Positive	18 (36%)
Negative	32 (64%)

Table 1: AML subtypes, patients' response to induction remission therapy, and aberrant expression of CD7 in 50 AML patients.

As shown in **Table 2**, CD7 expression was not significantly associated with AML subtype ($P = 0.904$).

Table 2: Association between aberrant CD7 expression and AML subtypes.

CD7 expression	AML subtypes		Total No. (%)	P-value
	Monocytic No. (%)	Non-monocytic No. (%)		
Positive	7 (35)	11 (36.7)	18 (36)	0.904
Negative	13 (65)	19 (63.3)	32 (64)	
Total	20	30	50	

Table 3 shows that 16 (88.9%) AML patients with positive CD7 expression had IR after induction remission therapy, with a significant association ($P =$

0.002) between failure of induction remission and aberrant CD7 expression in AML patients.

Table 3: Distribution of the AML cases by CD7 expression and responses to induction remission therapy.

Aberrant CD7 Expression	Response to treatment (Remission)		Total No. (%)	P-value
	Incomplete No. (%)	Complete No. (%)		
Positive	16 (88.9)	2 (11.1)	18 (36.0)	0.002
Negative	14 (43.8)	18 (56.2)	32 (64.0)	
Total	30	20	50	

Discussion

Leukemic blasts may have an "aberrant" immune pattern. This, along with molecular characterization of clonal breakpoints or mutations, could help separate entities with different prognoses and provide a more accurate picture of how well the treatment is working (2). The expression of CD7 is high in people with AML and is linked to lower remission rates and shorter life spans (9). CD7 was expressed in 10% to 40% of blasts from patients with AML. (10-12) The presence of CD7 on AML cells indicates that they are functionally immature and can be considered a risk factor for poor prognosis (13). There is some disagreement regarding the usefulness of CD7 expression as a prognostic marker in AML. It may have a negative, positive, or no effect (14-16).

In this study, the aberrant CD7 marker was expressed in 36% of cases, similar to other studies (5, 9, 17, 21). An Iraqi study reported that CD7 was the most commonly abnormally expressed marker in AML (25.7%), lower than that reported in the current study. It was followed by CD4 and CD19 (5). In a study in southern India, CD7 was found to be the most common lymphoid marker in 70.3% of AML patients. It was followed by CD19 (13.5%) and CD79a (10.8%), (17). Two studies by Raza *et al.* (30%) and Hussein *et al.* (60.7%) found similar results for high-level CD7 expression in AML to the current study. (19) Other studies, however, found lower rates of CD7 expression (16.7%, 18.1%, 25%, and 20%, respectively), (20-23).

No statistically significant association was found between abnormal CD7 expression and the two AML subtypes: monocytic and non-monocytic, in the current study. Other studies have found strong associations between non-monocytic AML subtypes. These include Raza's study on M2 (18) and Al-Anzi's study on M0

(5). Another study found that CD7 and TdT expression is higher in the AML-M0 group than in other AML subtypes (24).

The current study showed abnormal expression of CD7 in AML patients who did not respond to induction remission treatment. Similar studies have found that patients with CD7-positive AML do not respond well to standard AML chemotherapy and have poor outcomes (12).

One study in New Delhi investigated the prognostic significance of CD7 expression and its association with several factors, such as the level of low residual disease, the level of post-induction, the level of molecular status, and the level of cytogenetic prognosis. The study also observed overall survival, relapse rate, and time to free survival. It also examined leukemia-free survival and immune system changes associated with leukemia. The results showed that CD7 positivity was associated with the highest rates of relapse, MRD positivity, and death, indicating that patients with AML have a poor prognosis (25).

Limitations

The main limitation was its small sample size. Further research involving larger cohorts and long-term follow-up is required to validate and strengthen these findings.

Conclusion

CD7 was expressed in a substantial portion of AML patients. High levels of this lymphoid marker correlate with incomplete remission following induction therapy, portending poor prognosis.

Authors' declaration:

We can confirm that all of the tables in the paper are from this study. This study was approved by the Research Ethics Committee of the Medical City Hospital and the Pathology and Forensic Medicine Department at the University of AL-Iraqia College of Medicine. It ran from January 2019 to December 2020. All of the participants gave their informed permission. Number of ethical approval number was 96 on 22-4-2026.

Conflict of Interest: The authors declare no conflict of interest

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Data availability: The data supporting the findings of this study are available from the corresponding author upon reasonable request

Authors' contributions:

Study conception & design: (Sarab H. Moulod). Literature search: (Sarab H. Moulod). Data acquisition: (Sarab H. Moulod & Haithem A AL-Rubaie). Data analysis & interpretation: (Sarab H. Moulod & Haithem A AL-Rubaie). Manuscript preparation: (Sarab H. Moulod & Haithem A AL-Rubaie). Manuscript editing & review: (Haithem A AL-Rubaie).

AI declaration:

No artificial intelligence tools were used in the design, analysis, or writing of this manuscript.

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الاهمية الانذارية للتعبير عن مستضد (CD7) عند المرضى العراقيين المصابين بابيضاض الدم الحاد غير المسبوق

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خلفية البحث: يعتبر تعبير الخلايا التائية الليمفاوية السابع عاملاً انذارياً سلبياً. وقد تم تسجيل تعبيرات غير طبيعية لهذا العامل. تم تسجيل تعبيرات غير طبيعية للماركرات المظهرية في 88% من حالات ابيضاض الدم النقوي الحاد.

الأهداف: تقييم التعبير غير الطبيعي لـ CD7 في حالات البالغين المشخصة حديثاً بمرض ابيضاض الدم النقوي الحاد، وعلاقته بالاستجابة للعلاج الاستقرائي، وربطه بالأنواع الفرعية للمرض.

المنهجية: تم فحص عينات من الدم الكامل او سحب نخاع العظم لـ 50 مريض بالغ مصاب بلوكيميا الدم في مستشفى بغداد التعليمي / مدينة الطب باستخدام تقنية التدفق الخلوي للفترة من كانون الثاني الى كانون الاول 2019 تم تصنيف المرضى وفقاً لمعايير (FAB) إلى أنواع وحيدة الخلية وغير الوحيدة. استخدم اختبار "مربع كاي" الإحصائي لمقارنة المتغيرات المنفصلة غير الموزعة طبيعياً.

النتائج: من بين مرضى AML، وجد أن CD7 تم التعبير عنه في 36% من الحالات. وعانى 88.9% من أولئك الذين لديهم تعبير إيجابي لـ CD7 من شفاء غير كامل، مما أظهر ارتباطاً معنوياً كبيراً بين ضعف الاستجابة للعلاج الاستقرائي وتعبير CD7 بقيمة احتمالية لم يتم العثور على ارتباط ذو دلالة إحصائية بين تعبير CD7 والأنواع الفرعية لـ AML سواء كانت وحيدة الخلية أو غير وحيدة حيث كانت القيمة الاحتمالية وجدت الأنواع الفرعية غير الوحيدة في 30 مريضاً (60%)، بينما كان 20 مريضاً (40%) من النوعين M4 و M5 بعد العلاج الاستقرائي، حقق 20 مريضاً فقط 40% شفاء كاملاً، بينما كان لدى 30 مريضاً (60%) شفاء غير كامل.

الاستنتاج: ظهر تعبير CD7 بشكل متكرر في حالات ابيضاض الدم النقوي الحاد. ويرتبط التعبير العالي لهذا الماركر الليمفاوي لدى مرضى ابيضاض الدم النقوي الحاد بعدم اكتمال الاستجابة للعلاج الاستقرائي، وهو ما قد يؤدي إلى نتائج سريرية ضعيفة.

الكلمات المفتاحية: ابيضاض الدم النقوي الحاد، تعبير العامل الخلوي السابع، العلاج البدائي، الخلايا الاحادية، شفاء.