

# БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ

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**БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ**  
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**PROGNOSTIC SIGNIFICANCE OF CD123 (IL3RA) EXPRESSION IN PATIENTS WITH ACUTE LEUKEMIAS**

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 <http://dx.doi.org/10.5281/zenodo.19814283>**ABSTRACT**

This study evaluated the clinical and prognostic significance of CD123 (IL3RA) expression in patients with acute leukemia. A total of 116 patients were included in this single-center observational study. CD123 expression in bone marrow blast cells was assessed by multiparameter flow cytometry and quantified as the percentage of CD123-positive cells. CD123 expression was detected in 79.3% of patients, with high expression ( $\geq 50\%$ ) observed in 68.1%. The highest levels were found in myeloid, myelomonocytic, and monoblastic variants.

High CD123 expression was associated with increased bone marrow blast infiltration, aggressive disease course, primary resistance to therapy, and early relapse. A prognostic risk score incorporating CD123 expression, blast percentage, and leukemia subtype was developed and demonstrated acceptable predictive performance (AUC  $\approx 0.74$ ).

The findings support the inclusion of CD123 in routine immunophenotyping panels and highlight its role as a prognostic biomarker for risk stratification and individualized therapeutic decision-making in acute leukemia.

**Key words:** CD123, interleukin-3, acute lymphoblastic leukemia, acute myeloid leukemia.

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**О‘TKIR LEYKOZLARDA CD123 (IL3RA) EKSPRESSIYASINING PROGNOSTIK AHAMIYATI****ANNOTATSIYA**

Tadqiqotning maqsadi o‘tkir leykozlar bilan og‘rigan bemorlarda CD123 (IL3RA) ekspressiyasining klinik va prognostik ahamiyatini baholashdan iborat bo‘ldi. Bir markazli kuzatuv tadqiqotiga 116 nafar bemor kiritildi. Suyak iligi blast hujayralarida CD123 ekspressiyasi ko‘p rangli oqim sitometriyasi usuli yordamida aniqlandi. CD123 79,3% bemorlarda aniqlanib, yuqori ekspressiya

( $\geq 50\%$ ) 68,1% holatda qayd etildi. Eng yuqori ko'rsatkichlar miyeloid, miyelomonotsitar va monoblast variantlarda kuzatildi.

CD123 yuqori darajasi kasallikning agressiv kechishi, davolashga birlamchi rezistentlik, erta relapslar va suyak iligida yuqori blast infiltratsiyasi bilan bog'liq ekanligi aniqlandi. CD123 darajasi, blastlar foizi va leykoz turi asosida prognozlash shkalasi ishlab chiqildi va model qoniqarli prognoz aniqligini ko'rsatdi (AUC  $\approx 0,74$ ).

Olingan natijalar CD123 ni standart immunofenotiplash panellariga kiritish zarurligini va uni o'tkir leykozlarda xavf stratifikatsiyasi hamda individual davolash taktikasini tanlashda muhim biomarker sifatida qo'llash mumkinligini ko'rsatadi.

**Kalit so'zlar:** CD123, interleykin-3, o'tkir limfoblast leykoz, o'tkir miyeloid leykoz.

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## ПРОГНОСТИЧЕСКОЕ ЗНАЧЕНИЕ ЭКСПРЕССИИ CD123 (IL3RA) У ПАЦИЕНТОВ С ОСТРЫМИ ЛЕЙКОЗАМИ

### АННОТАЦИЯ

Целью исследования явилась оценка клинико-прогностического значения экспрессии CD123 (IL3RA) у пациентов с острыми лейкозами. В одноцентровое наблюдательное исследование включено 116 пациентов. Экспрессия CD123 в бластных клетках костного мозга определялась методом многоцветной проточной цитометрии. CD123 выявлен у 79,3% пациентов, при этом высокая экспрессия ( $\geq 50\%$ ) зарегистрирована у 68,1%. Наиболее выраженная экспрессия отмечалась при миелоидных, миеломоноцитарных и монобластных вариантах острых лейкозов.

Высокий уровень CD123 ассоциировался с неблагоприятными исходами лечения, включая первичную резистентность, ранние рецидивы и агрессивное течение заболевания. Разработана прогностическая шкала риска, включающая уровень CD123, степень бластной инфильтрации костного мозга и морфологический вариант лейкоза. Модель показала удовлетворительную прогностическую точность (AUC  $\approx 0,74$ ).

Полученные данные подтверждают целесообразность включения CD123 в стандартные панели иммунологической диагностики и его использование как биомаркера для стратификации риска и персонализации терапии у пациентов с острыми лейкозами.

**Ключевые слова:** CD123, интерлейкин-3, острый миелоидный лейкоз, острый лимфобластный лейкоз.

So'nggi yillarda leykoz hujayralari yuzasida ifodalangan immunologik markerlarga alohida e'tibor qaratildi, ular o'sma klonining biologik xususiyatlarini aks ettiradi va potentsial terapevtik maqsadlar deb hisoblanishi mumkin. Bunday markerlardan biri CD123, interleykin-3 retseptorining (IL3RA)  $\alpha$ -zanjiridir. CD123 odatda cheklangan miqdordagi gematopoetik hujayralarda, jumladan, erta miyeloid hujayralari va plazmatsitoid dendritik hujayralarda ifodalanadi, shu bilan birga uning ifodasi o'tkir leykemiya sezilarli darajada oshadi.

CD123 ekspressiyasining ortishi asosan o'tkir miyeloid leykemiya, jumladan, mielomonotsitik va monoblastik variantlarda, shuningdek, bir qator limfoid shakllarda tasvirlangan. Eksperimental va klinik tadqiqotlar shuni ko'rsatadiki, CD123 leykemik ozak hujayralarida faol ravishda ifodalanadi, ular dori rezistentligi rivojlanishida va kasallikning qaytalanishida muhim rol o'ynaydi. Interleykin-3 retseptorlari bilan bog'liq signal yo'llarining faollashishi o'sma hujayralarining ko'payishini rag'batlantiradi va leykemiyaning agressiv klinik kechishining asosini tashkil etuvchi apoptozni bostiradi.

To'plangan ma'lumotlar CD123 ning yuqori ifodalanishi va yomon prognoz, to'liq remissiya darajasining pasayishi va qaytalanish xavfining ortishi o'rtasidagi mumkin bo'lgan bog'liqlikni ko'rsatadi. Biroq, tadqiqot natijalari namunalarning heterogenligi, CD123 ifodasini baholash usullaridagi farqlar va suyak iligi blast infiltratsiyasi darajasi va qo'llanilgan davolash rejimlari kabi klinik va laboratoriya omillarining yetarlicha hisobga olinmasligi tufayli aniq emas.

Shuning uchun, o'tkir leykemiya bilan og'rigan bemorlarda CD123 ekspressiyasini kasallikning morfologik turi, suyak iligi blast darajasi, qo'llaniladigan polikemoterapiyaning tabiati va davolash natijalarini hisobga olgan holda keng qamrovli o'rganish dolzarbdir. Ushbu yondashuv CD123 ning prognostik ahamiyatini va uning xavfni stratifikatsiya qilish va terapevtik strategiyani tanlashdagi potentsial rolini chuqurroq baholash imkonini beradi.

**Buning maqsadi** Tadqiqotning maqsadi kasallikning morfologik variantiga, suyak iligining blast infiltratsiyasi darajasiga, qo'llanilgan polikimyoterapiya rejimlariga va davolash natijalariga qarab, o'tkir leykemiya bilan og'rigan bemorlarda CD123 (IL3RA) ekspressiyasining klinik va prognostik ahamiyatini baholash .

**Materiallar va usullar.** Tadqiqot dizayni va bemorning xususiyatlari. Bu ixtisoslashgan gematologiya shifoxonasida baholash va davolanayotgan o'tkir leykemiya bilan og'rigan bemorlarni o'z ichiga olgan yagona markazli, kuzatuv tadqiqoti hisoblanadi. Tahlilga morfologik va immunologik suyak iligi tekshiruvini o'z ichiga olgan keng qamrovli klinik va laboratoriya tekshiruvidan o'tgan 116 bemor kiritilgan.

Tadqiqotga kiritish mezonlari quyidagilar : morfologik va immunologik ma'lumotlarga asoslangan o'tkir leykemiya tashxisi tasdiqlangan, CD123 ekspressiyasini baholovchi oqim sitometriyasi natijalari va davolash natijalari bo'yicha klinik ma'lumotlarning mavjudligi. Tadqiqotdan chiqarilgan mezonlari to'liq bo'lmagan klinik va laboratoriya ma'lumotlari va immunologik test natijalarining yo'qligini o'z ichiga oldi.

Tadqiqot guruhida o'tkir leykemiyaning turli morfologik variantlarini, jumladan, o'tkir miyeloid leykemiya, o'tkir mielomonotsitik va monoblastik variantlarni, B- va T-hujayrali o'tkir limfoblastik leykemiya, shuningdek, promyelotsitik va differentsiatsiyalanmagan leykemiyaning alohida holatlarini o'z ichiga olgan. Barcha bemorlarga suyak iligining blast infiltratsiyasi darajasi baholandi, bu yadroli hujayralar umumiy soniga nisbatan foiz sifatida ifodalangan.

Davolash strategiyalari bemorning klinik holati, yoshi va kasallikning morfologik turiga qarab belgilandi va intensiv va past intensivlikdagi polikimyoterapiya rejimlarini o'z ichiga oldi. Davolash natijalari klinik va gematologik mezonlar asosida baholandi va to'liq gematologik remissiya, kasallikning qaytalanishi, birlamchi refrakter yoki refrakter kasallik, shuningdek, o'lim yoki davolashning muvaffaqiyatsizligi sifatida tasniflandi.

Oqim sitometriyasi va CD123 ekspressiyasini baholash. Suyak iligi hujayralarining immunofenotiplanishi ko'p rangli oqim sitometriyasi va standart antitelo monoklonal panellari yordamida amalga oshirildi. Maxsus terapiya boshlanishidan oldin olingan suyak iligi aspiratsiyalari tadqiqot materiali bo'lib xizmat qildi.

Blast populyatsiyasini aniqlash uchun antigenlarning kombinatsiyasi, jumladan, CD45 va CD45/SSC koordinatalaridan foydalangan holda hujayra taqsimoti tahlili, shuningdek, miyeloid va limfoid differentsiatsiyasining nasl-nasabga xos markerlari qo'llanildi. CD123 ekspressiyasi darvozali blast hujayralari populyatsiyasida baholandi.

CD123 ifodasi CD123-musbat hujayralarning foizi sifatida aniqlandi va miqdoriy ma'lumotlar mavjud bo'lganda, qo'shimcha ravishda lyuminesentsiya intensivligi bo'yicha baholandi. Sifatli ifodani baholash holatlarida natijalar salbiy, o'rtacha ijobiy yoki ijobiy deb tasniflandi. Statistik tahlil uchun CD123 ifodasi standartlashtirildi va ikkilik o'zgaruvchi sifatida taqdim etildi, past (<50%) va yuqori (≥50%) ifoda guruhlari aniqlandi.

Olingan ma'lumotlar CD123 ekspressiyasi va leykemiyaning morfologik varianti o'rtasidagi bog'liqlikni, suyak iligining blast infiltratsiyasi darajasini va davolashning klinik natijalarini tahlil qilish uchun ishlatilgan.

**Natijalar.** Tadqiqotda o'tkir leykemiya bilan kasallangan 116 bemor ishtirok etdi. Bemorlarning yoshi 18 yoshdan 78 yoshgacha bo'lgan, o'rtacha yoshi 46 yoshni tashkil etgan (IQR 34–59). Oltmish yetti nafari (57,8%) ayollar va 49 nafari (42,2%) erkaklar edi. Kasallikning morfologik variantlariga ko'ra, namunaviy tuzilmada o'tkir leykemiyaning miyeloid shakllari ustunlik qildi va 65 (56,0%) bemorda tashxis qo'yildi. Variant ko'rsatilmagan o'tkir miyeloid leykemiya 33 (28,4%) bemorda, o'tkir mielomonotsitik leykemiya 22 (19,0%) va OML ning monoblastik varianti 10 (8,6%) bemorda aniqlandi. O'tkir limfoblastik leykemiya 40 (34,4%) bemorda tashxis qo'yildi, ulardan B-hujayrali variant 36 (31,0%) va T-hujayrali variant 4 (3,4%) bemorda aniqlandi. O'tkir promyelotsitik leykemiya 5 (4,3%) bemorda aniqlandi. Bemorlarning morfologik variantlar bo'yicha taqsimoti 1-jadvalda keltirilgan.

Tashxis	n	%
OML	33	28.4
OMML	22	19.0
OML, monoblastik	10	8.6
<b>Barcha miyeloid shakllari (jami)</b>	<b>65</b>	<b>56.0</b>
B-OLL	36	31.0
T-OLL	4	3.4
OPL	5	4.3
Boshqalar	4	3.3

Suyak iligining blast infiltratsiyasi darajasini tahlil qilish shuni ko'rsatdiki, kasallik ko'pchilik bemorlarda sezilarli darajada blast bilan boshlangan. Blast hujayralarining o'rtacha soni 82% ni tashkil etdi (IQR 65–92), bemorlarning taxminan 78% ida blast darajasi 50% dan oshdi, bu tashxis qo'yilganda o'sma yukining yuqori ekanligini ko'rsatadi. Umumiy bemorlar guruhida CD123 ifodasi. CD123 ifodasi 116 bemordan 92 tasida (79,3%) aniqlangan, CD123 fenotipi esa 24 bemorda (20,7%) salbiy qayd etilgan. CD123 ifodasini miqdoriy aniqlashda median qiymati 70% ni (IQR 50–90) tashkil etdi, diapazoni 20 dan 100% gacha.

Morfologik variant	n	CD123 <sup>+</sup> , n (%)	Mediana CD123, % (IQR)	Yuqori CD123 ifodasi ≥50%, n (%)
OML	33	28 (84,8%)	75 (60–90)	24 (72,7%)
OMML	22	20 (90,9%)	80 (65–95)	18 (81,8%)
OML, monoblastik	10	10 (100%)	90 (70–95)	9 (90,0%)
OPL	5	4 (80,0%)	55 (40–70)	3 (60,0%)
B-OLL	36	24 (66,7%)	50 (30–70)	18 (50,0%)
T-O	4	1 (25,0%)	30 (20–40)	1 (25,0%)
Boshqa shakllar*	6	2 (33,3%)	35 (25–45)	2 (33,3%)
<b>Jami</b>	<b>116</b>	<b>92 (79,3%)</b>	<b>70 (50–90)</b>	<b>79 (68,1%)</b>

Keyingi tahlil uchun bemorlar CD123 ekspressiyasi past (<50%) va yuqori (≥50%) guruhlarga bo'lindi. 79 (68,1%) bemorda yuqori CD123 ekspressiyasi, 37 (31,9%) bemorda past ekspressiya aniqlandi.

CD123 ifodalanishi va leykemiyaning morfologik varianti. CD123 ifodalanishining chastotasi va darajasi kasallikning morfologik variantiga sezilarli darajada bog'liq edi (2-jadval). CD123 ning eng yuqori ifodalanishi o'tkir leykemiyaning miyeloid shakllarida kuzatildi. Shunday qilib, CD123-musbat fenotip OML bilan og'rigan bemorlarning 84,8% da, OMML bilan og'rigan bemorlarning 90,9% da va OML ning monoblastik varianti bilan og'rigan bemorlarning 100% da aniqlandi. Bundan

tashqari, CD123 ning yuqori ifodalanishi ( $\geq 50\%$ ) tegishli kichik guruhlardagi bemorlarning 72,7%, 81,8% va 90,0% da qayd etildi.

O'tkir limfoblastik leykemiyada CD123 ekspressiyasi ko'proq o'zgaruvchan bo'lgan. B-ALL guruhida CD123 bemorlarning 66,7 foizida aniqlangan, ammo yuqori ekspressiya atigi 50,0 foizda kuzatilgan. T-hujayrali OLLda CD123 ekspressiyasi sezilarli darajada kamroq uchraydi - bemorlarning 25,0 foizida - va past qiymatlar bilan tavsiflangan.

Chiqish	n	%
KGR (jami)	58	50
— qaytalanish yo'q	39	34
— qaytalanish bilan	19	16
Birlamchi chidamlilik kursi	24	21
Rezistentlik/progressivlik	19	16
O'lim / MTA	7	6
Rad etilgan	9	7

Shunday qilib, CD123 ning yuqori ifodalanishi o'tkir leykemiyaning miyeloid variantlarida limfoid shakllarga qaraganda ancha tez-tez aniqlandi.

**Munozara.** Ushbu tadqiqotda o'tkir leykemiya bilan og'rigan bemorlarda CD123 (IL3RA) ekspressiyasining keng qamrovli tahlili o'tkazildi, bunda kasallikning morfologik turi, suyak iligining blast infiltratsiyasi darajasi, qo'llanilgan davolash rejimlari va klinik natijalar hisobga olindi. Natijalar CD123 ning yuqori biologik va prognostik ahamiyatini tasdiqlaydi va uning o'tkir leykemiyaning agressiv kechishidagi roli haqidagi tushunchamizni kengaytiradi.

Tadqiqot kohortasida bemorlarning aksariyat qismida CD123 ekspressiyasi aniqlandi, bemorlarning uchdan ikki qismidan ko'prog'ida yuqori ekspressiya ( $\geq 50\%$ ) kuzatildi. Ushbu ma'lumotlar ilgari nashr etilgan tadqiqotlarga mos keladi, ko'rsatilishicha, CD123 o'tkir miyeloid leykemiyada, ayniqsa mielomonotsitik va monoblastik variantlarda keng tarqalgan. Bizning tadqiqotimizda AML ning monoblastik shakllarida kuzatilgan eng yuqori CD123 ekspressiyasi ushbu markerning erta va kamroq differentsiatsiyalangan o'sma hujayralari bilan chambarchas bog'liqligi haqidagi gipotezani qo'llab-quvvatlaydi.

Shu bilan birga, o'tkir leykemiyaning limfoid shakllarida, ayniqsa ALL ning T-hujayrali variantida, CD123 ekspressiyasi sezilarli darajada kamroq aniqlandi va pastroq qiymatlar bilan tavsiflandi. B-ALL da CD123 ekspressiyasidagi shunga o'xshash o'zgaruvchanlik boshqa mualliflar tomonidan tasvirlangan, bu limfoid o'sma klonlarining biologik heterojenligini va ularning omon qolishini qo'llab-quvvatlovchi signalizatsiya yo'llaridagi farqlarni aks ettirishi mumkin.

### Oqibati yomon natija xavfi uchun prognostik shkala

Parametr	Mezon	Ballar
CD123 ifodasi	<50%	0
	$\geq 50\%$	2
Suyak iligi blastlari	<50%	0
	$\geq 50\%$	1
Morfologik variant	Limfoid (OLL)	0
	Miyeloid (OML, OMML, monoblastik)	1

### Shkala talqini (xavf guruhlari)

<p>➤ <b>Past xavf (0–1 ball)</b></p> <ul style="list-style-type: none"> <li>✓ Doimiy KGR ehtimoli yuqori</li> <li>✓ Birlamchi qarshilikning past xavfi</li> <li>✓ Standart terapiya, standart monitoring</li> </ul> <p>➤ <b>O'rtacha xavf (2 ball)</b></p> <ul style="list-style-type: none"> <li>✓ Qaytalanish xavfi o'rtacha</li> <li>✓ Keyinchalik javob yo'qolishi bilan KGR mumkin</li> <li>✓ MRB monitoringi va baholashni kuchaytirish</li> </ul> <p>➤ <b>Yuqori xavf (3-4 ball)</b></p> <ul style="list-style-type: none"> <li>• Yuqori chastota:             <ul style="list-style-type: none"> <li>✓ birlamchi qarshilik</li> <li>✓ erta relaps</li> </ul> </li> <li>• Kasallikning agressiv yo'nalishi             <ul style="list-style-type: none"> <li>✓ alternativ sxemalar</li> <li>✓ CD123-maqsadli terapiya</li> </ul> </li> </ul>	<p><b>1-qadam.</b> Oqim sitometriyasi yordamida CD123 ifodasini (%) aniqlang</p> <ul style="list-style-type: none"> <li>• <math>\geq 50\%</math> → +2 ball</li> <li>• <math>&lt; 50\%</math> → 0 ball</li> </ul> <p><b>2-qadam.</b> Suyak iligining blast infiltratsiyasini baholash</p> <ul style="list-style-type: none"> <li>• <math>\geq 50\%</math> → +1 ball</li> <li>• <math>&lt; 50\%</math> → 0 ball</li> </ul> <p><b>3-qadam.</b> Leykemiyaning morfologik variantini aniqlang</p> <ul style="list-style-type: none"> <li>• OML / OMML / monoblastik → +1 ball</li> <li>• BARCHA → 0 ball</li> </ul> <p><b>4-qadam.</b> Ballarni umumlashtiring → xavf guruhini aniqlang</p> <ul style="list-style-type: none"> <li>• 0–1 → past</li> <li>• 2 → oraliq</li> <li>• 3–4 → yuqori</li> </ul>
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Ishlab chiqilgan prognostik shkalaning ROC tahlili salbiy davolash natijalari uchun qoniqarli diskriminatsiya qobiliyatini ko'rsatdi ( $AUC \approx 0.74$ ,  $p < 0.01$ ). Optimal chegara  $\geq 3$  ball bo'lib, bunda modelning sezgirligi va o'ziga xosligi mos ravishda taxminan 72% va 68% ni tashkil etdi. Ushbu ma'lumotlar o'tkir leykemiya bilan og'rigan bemorlarda erta xavf stratifikatsiyasi uchun taklif qilingan shkalaning amaliy qo'llanilishi salohiyatini namoyish etadi.

**Xulosa.** Tadqiqot o'tkir leykemiya bilan og'rigan bemorlarda CD123 (IL3RA) ekspressiyasining yuqori klinik va prognostik ahamiyatini ko'rsatdi. CD123 o'tkir leykemiyada, asosan miyeloid, mielomonotsitik va monoblastik variantlarda keng ifodalanganligi va suyak iligining yuqori darajadagi blast infiltratsiyasi bilan bog'liqligi aniqlandi.

Yuqori CD123 ifodasi ( $\geq 50\%$ ) davolashning salbiy natijalari, jumladan, birlamchi qarshilik, qaytalanish va kasallikning rivojlanishi bilan sezilarli darajada bog'liqligi ko'rsatilgan. Yuqori CD123 darajasiga ega bemorlar kasallikning yanada agressiv kechishi va standart polikemoterapiya samaradorligining pasayishi bilan tavsiflangan.

Olingan ma'lumotlar asosida, CD123 ekspressiyasi, suyak iligi blast infiltratsiyasi darajasi va leykemiyaning morfologik turini o'z ichiga olgan nojo'ya natijalar xavfi uchun prognostik bal ishlab chiqildi va tasdiqlandi. Taklif etilgan model qoniqarli diskriminatsiya qobiliyatini namoyish etdi va past, o'rta va yuqori prognostik xavf guruhlarini aniqlash imkonini berdi.

Olingan natijalar o'tkir leykemiyaning birlamchi tashxislash uchun standart immunoassay panellariga CD123 ni kiritish maqsadga muvofiqligini asoslaydi va xavfni stratifikatsiya qilish va davolashni optimallashtirish uchun CD123 dan biomarker sifatida foydalanish imkoniyatini tasdiqlaydi. Ishlab chiqilgan prognostik shkaladan foydalanish kasallikning noqulay kechishi xavfi yuqori bo'lgan bemorlarni erta aniqlashga yordam beradi va individual terapevtik yondashuvlarni, shu jumladan maqsadli yondashuvlarni qo'llashni qo'llab-quvvatlaydi.

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