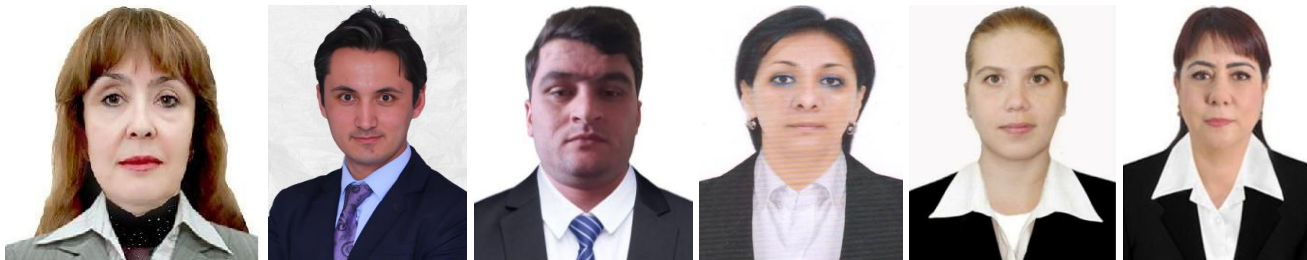


PATIENT REFERRAL PATHWAYS AND DIAGNOSTIC TIMING OF ACUTE LEUKEMIA IN CHILDREN IN TAJIKISTAN



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СХЕМЫ НАПРАВЛЕНИЯ ПАЦИЕНТОВ И СРОКИ ДИАГНОСТИКИ ОСТРОГО ЛЕЙКОЗА У ДЕТЕЙ В ТАДЖИКИСТАНЕ

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Резюме. Ўткир лейкемия болалик даврида ҳаммадан кўра кўпроқ учрайдиган хавфли касаллик бўлиб ҳисобланади ва касалланиш ҳамда ўлим ҳолларининг асосий сабабларидан бири бўлиб қолади. Даволаш соҳасидаги ютуқлар юқори даромадли мамлакатларда яшаб қолиш кўрсаткичларини сезиларли даражада яхшилаган бўлса-да, паст ва ўрта даромадли мамлакатларда даволаш натижалари ҳали ҳам орқада қолмоқда. Энг муҳим прогностик омиллардан бири ўз вақтида таъхис қўйиш бўлиб, кўплаб минтақаларда соғлиқни сақлаш тизимини ташкил этиш ва ихтисослаштирилган тиббий ёрдамдан фойдаланиш таъсир кўрсатади. Ўртача умумий диагностика оралиги $45,2 \pm 12,8$ кунни ташкил этди. Энг узоқ кечикишлар ихтисослашишдан олдинги босқичда, айниқса, шифокорга биринчи мурожаат қилиш ва болалар гематологи йўлланмаси ўртасида кузатилди. Таъхис қўйишнинг кечикишини башорат қилувчи муҳим омилларга бирламчи тиббий ёрдам муассасаларига биринчи марта мурожаат қилиш (ОШ 2,8; 95% ДИ 1,9–4,1), дастлабки текширувда тўлиқ қон таҳлилининг йўқлиги (ОШ 3,2; 95% ДИ 2,1–4,9), қишлоқ жойларда яшаш (ОР 2,1; 95% ДИ 1,4–3,2) ва периферик тиббиёт муассасаларида автоматик гематологик анализаторларнинг чекланганлигининг мавжудлиги (ОР 3,8; 95% ДИ 2,5–5,4) киради. Тоҷикистонда ўткир лейкемия билан оғриган болалар, асосан, соғлиқни сақлаш тизимидаги таъхилий ва инфратузилма чекловлари туфайли диагностикада сезиларли кечикишларга дуч келишмоқда. Бирламчи тиббий ёрдам даражасида эрта таъхисни яхшилаш, диагностика алгоритмларини стандартлаштириш ва асосий лаборатория диагностикасига киришни кенгайтириш диагностика кечикишларини сезиларли даражада камайтириши ва клиник натижаларни яхшилаши мумкин.

Abstract. Acute leukemia is the most common malignant disease in childhood and remains a major cause of morbidity and mortality. Although advances in treatment have significantly improved survival in high-income countries, outcomes in low- and middle-income settings continue to lag behind. One of the most important prognostic determinants is the timeliness of diagnosis, which in many regions is influenced by healthcare system organization and access to specialized care. The median overall diagnostic interval was 45.2 ± 12.8 days. The longest delays occurred at the pre-specialist stage, particularly between initial medical contact and referral to a pediatric hematologist. Significant predictors of diagnostic delay included first presentation at primary healthcare facilities (OR 2.8; 95% CI 1.9–4.1), absence of a complete blood count at initial evaluation (OR 3.2; 95% CI 2.1–4.9), rural residence (OR 2.1; 95% CI 1.4–3.2), and limited availability of automated hematology analyzers in peripheral medical institutions (OR 3.8; 95% CI 2.5–5.4). Children with acute leukemia in Tajikistan experience substantial delays in diagnosis, primarily due to organizational and infrastructural limitations within the healthcare system. Improving early recognition at the primary care level, standardizing diagnostic algorithms, and expanding access to basic laboratory diagnostics may significantly reduce diagnostic delays and improve clinical outcomes.

Keywords: Acute leukemia; pediatric oncology; diagnostic delay; referral pathways; primary healthcare; Tajikistan.

Introduction. Acute leukemia remains the most common malignant disease in childhood and continues to pose significant diagnostic and therapeutic challenges worldwide. In pediatric populations, acute leukemias account for approximately one third of all malignant neoplasms [2, 4]. While modern treatment protocols have led to excellent outcomes in many countries, with long-term survival in acute lymphoblastic leukemia approaching 90%, such results are not uniformly achievable across all healthcare systems [1].

In the Republic of Tajikistan, survival outcomes for children with acute leukemia remain noticeably lower than those reported in high-income countries [5, 11]. One of the most important factors influencing prognosis is the timeliness of diagnosis. Delays in establishing the diagnosis have been shown to negatively affect survival, with postponement beyond four weeks associated with a clinically meaningful reduction in treatment outcomes [6,10]. In resource-limited settings, diagnostic delay is often multifactorial and reflects not only clinical complexity but also organizational constraints within the healthcare system [3, 8].

The diagnostic pathway in Tajikistan is shaped by several region-specific factors, including geographic dispersion of the population, limited access to specialized care, uneven availability of diagnostic equipment, and sociocultural influences on healthcare-seeking behavior [7, 9]. Understanding how these factors interact is essential for identifying weaknesses in the current system and developing realistic, locally applicable solutions.

Aim. The aim of this study was to analyze patient referral pathways and determine how organizational and clinical factors influence the time to diagnosis of acute leukemia in children in the Republic of Tajikistan.

Materials and Methods. A retrospective cohort analysis was performed at the National Medical

Center of the Republic of Tajikistan. Medical records of pediatric patients treated between January 2024 and November 2025 were reviewed. The study included 40 children aged 2 to 16 years with a confirmed diagnosis of acute leukemia based on morphological examination of bone marrow samples.

Among the enrolled patients, 25 children (62.5%) were diagnosed with acute lymphoblastic leukemia, while 15 patients (37.5%) had acute myeloid leukemia. For each case, the diagnostic timeline was reconstructed, starting from the first appearance of symptoms to final verification of the diagnosis. Time intervals between key diagnostic stages were analyzed. Statistical evaluation included descriptive analysis and multivariate logistic regression to identify factors associated with prolonged diagnostic intervals. A p-value below 0.05 was considered statistically significant.

Results. The analysis revealed that one of the central factors influencing diagnostic delays in Tajikistan is the highly uneven distribution of pediatric hematology specialists. Pediatric hematologists are concentrated almost exclusively in major urban centers. In Khatlon Region and the Gorno-Badakhshan Autonomous Oblast, such specialists are entirely absent. In Sughd Region, only four pediatric hematologists are available, which is insufficient for the population served. As a result, Dushanbe functions as the primary national referral center, hosting ten pediatric hematologists and receiving patients from across the country.

This workforce imbalance leads to a multi-step referral process. Children from peripheral regions are usually first assessed by non-specialist physicians, most commonly pediatricians or infectious disease specialists. Due to the nonspecific nature of early leukemia symptoms, this often results in delayed suspicion of a malignant process.

Table 1. Diagnostic intervals in pediatric acute leukemia (n=40)

No	Diagnostic stage	Median (days)	SD	IQR
1	Symptom onset to first medical consultation	18.3	±8.4	10.1–26.7
2	First consultation to hematologist referral	15.2	±6.7	8.7–21.9
3	Suspicion of leukemia to diagnostic confirmation	11.7	±4.3	7.4–16.0
Total diagnostic interval		45.2	±12.8	32.4–58.0

Table 2. Factors associated with prolonged diagnostic delay

No	Factor	Odds Ratio	95% CI	p-value
1	Initial contact at primary healthcare level	2.8	1.9–4.1	<0.001
2	No CBC performed at first visit	3.2	2.1–4.9	<0.01
3	Rural residence	2.1	1.4–3.2	<0.05
4	Absence of 5-part differential analyzers	3.8	2.5–5.4	<0.001

Subsequent referral to specialized centers requires additional time for coordination, transportation, and scheduling, further extending the diagnostic interval and postponing initiation of definitive therapy.

The median total time from symptom onset to confirmed diagnosis was 45.2 ± 12.8 days. Analysis of individual diagnostic stages demonstrated significant variability, with the longest delays occurring prior to hematologist consultation.

The initial delay, from symptom onset to first medical contact, was primarily influenced by the nonspecific nature of early clinical manifestations. Symptoms such as fatigue, pallor, and prolonged fever were often not perceived as alarming. Additional contributing factors included low health literacy, use of traditional medicine prior to seeking formal care, and socioeconomic limitations.

At the level of primary care, the median time from first consultation to referral to a hematologist was 15.2 ± 6.7 days. A major contributor to this delay was the absence of a complete blood count with leukocyte differential at the initial visit. In more than half of the cases, laboratory evaluation was not performed despite the presence of symptoms potentially suggestive of hematologic disease. Only one third of primary care physicians ordered blood tests when confronted with persistent asthenia, unexplained fever, or pallor.

Once leukemia was suspected, the time required for morphological verification of the diagnosis averaged 11.7 ± 4.3 days. Children from rural areas experienced significantly longer diagnostic timelines compared to urban patients, reflecting differences in access to diagnostic facilities and laboratory infrastructure.

Assessment of diagnostic capacity across healthcare levels revealed substantial disparities. While national referral centers were fully equipped, regional and district hospitals often lacked essential diagnostic tools, including automated hematology analyzers and facilities for bone marrow examination.

Discussion. The findings of this study highlight systemic weaknesses in the diagnostic pathway

for pediatric acute leukemia in Tajikistan. Diagnostic delays arise from a combination of clinical, organizational, and infrastructural factors. Limited access to specialists, insufficient laboratory capacity at peripheral levels, and lack of standardized diagnostic approaches at primary care all contribute to prolonged time to diagnosis.

Importantly, many of the identified barriers are potentially modifiable. Early recognition of leukemia relies heavily on simple and widely available tests, particularly the complete blood count. However, without clear clinical algorithms and adequate diagnostic support, opportunities for early detection are frequently missed.

Conclusion. Children with acute leukemia in Tajikistan experience considerable delays in diagnosis, with a median diagnostic interval exceeding six weeks. These delays are largely driven by structural and organizational deficiencies within the healthcare system, rather than by disease-related factors alone. Addressing these challenges will require a coordinated approach that includes education of primary care physicians, implementation of standardized diagnostic pathways, development of efficient referral systems, and gradual strengthening of laboratory infrastructure at regional and district levels.

Further studies should focus on evaluating the impact of such interventions on diagnostic timelines, treatment outcomes, and overall survival in pediatric acute leukemia.

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СХЕМЫ НАПРАВЛЕНИЯ ПАЦИЕНТОВ И СРОКИ ДИАГНОСТИКИ ОСТРОГО ЛЕЙКОЗА У ДЕТЕЙ В ТАДЖИКИСТАНЕ

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Резюме. Острая лейкемия является наиболее распространенным злокачественным заболеванием в детском возрасте и остается одной из основных причин заболеваемости и смертности. Несмотря на то, что достижения в области лечения значительно улучшили показатели выживаемости в странах с высоким уровнем дохода, результаты лечения в странах с низким и средним уровнем дохода по-прежнему отстают. Одним из важнейших прогностических факторов является своевременность диагностики, на которую во многих регионах влияют организация системы здравоохранения и доступ к специализированной медицинской помощи. Средний общий диагностический интервал составил $45,2 \pm 12,8$ дней. Наиболее длительные задержки наблюдались на доспециализированном этапе, особенно между первым обращением к врачу и направлением к детскому гематологу. К значимым факторам, предсказывающим задержку диагностики, относились первое обращение в учреждения первичной медицинской помощи (ОШ 2,8; 95% ДИ 1,9–4,1), отсутствие полного анализа крови при первоначальном обследовании (ОШ 3,2; 95% ДИ 2,1–4,9), проживание в сельской местности (ОР 2,1; 95% ДИ 1,4–3,2) и ограниченная доступность автоматических гематологических анализаторов в периферийных медицинских учреждениях (ОР 3,8; 95% ДИ 2,5–5,4). Дети с острым лейкозом в Таджикистане сталкиваются со значительными задержками в диагностике, в первую очередь из-за организационных и инфраструктурных ограничений в системе здравоохранения. Улучшение ранней диагностики на уровне первичной медицинской помощи, стандартизация диагностических алгоритмов и расширение доступа к базовой лабораторной диагностике могут значительно сократить задержки в диагностике и улучшить клинические результаты.

Ключевые слова: Острая лейкемия; детская онкология; задержка диагностики; пути направления к специалистам; первичная медицинская помощь; Таджикистан.