PHASES OF CHRONIC MYELOID LEUKEMIA AND EPIDEMIOLOGY IN UZBEKISTAN

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Abstract

This article presents a comprehensive and detailed analysis of chronic myeloid leukemia (CML), focusing on its three well-defined clinical and laboratory phases: the chronic phase, accelerated phase, and blast crisis. Each phase is examined in terms of its pathophysiological characteristics, blast cell percentage, peripheral blood and bone marrow morphology, hematological parameters, and associated cytogenetic abnormalities. Clinical manifestations, including fatigue, splenomegaly, anemia, thrombocytopenia, bleeding tendencies, and extramedullary infiltration, are described for each stage. The study also discusses current therapeutic approaches, including targeted tyrosine kinase inhibitors, chemotherapy, and supportive care, along with the prognostic significance of phase identification in guiding patient management.

In addition to the clinical and laboratory analysis, the study provides epidemiological insights into CML in the Republic of Uzbekistan, highlighting the annual incidence, age distribution, gender patterns, and the relative frequency of each disease phase. The analysis identifies that the majority of patients are diagnosed during the chronic phase, while a smaller proportion present in the accelerated phase or blast crisis. These findings emphasize the importance of early detection, accurate staging, and phase-specific treatment strategies to improve survival outcomes and quality of life for patients.

Furthermore, the article underscores the role of robust national registries and systematic data collection in monitoring disease trends, optimizing healthcare

resources, and developing effective public health strategies for hematologic malignancies in Uzbekistan. By integrating clinical, laboratory, and epidemiological perspectives, this study provides a comprehensive framework for clinicians, researchers, and policymakers to enhance diagnostic accuracy, tailor individualized therapies, and implement preventive interventions for CML.

Keywords: chronic myeloid leukemia, blast crisis, accelerated phase, chronic phase, epidemiology, Uzbekistan, clinical-laboratory phase, blast cell percentage

Introduction (Expanded Version)

Chronic myeloid leukemia (CML) is a clonal hematologic malignancy of the myeloid lineage, characterized by the uncontrolled proliferation of granulocytic cells in the bone marrow, typically driven by the BCR-ABL1 fusion gene resulting from the t(9;22)(q34;q11) chromosomal translocation, also known as the Philadelphia chromosome. This genetic abnormality leads to constitutive tyrosine kinase activity, which plays a central role in dysregulated cell proliferation, impaired apoptosis, and altered hematopoiesis.

The clinical course of CML is generally indolent in the early stages, but the disease can progress over time through three well-defined phases:

1. Chronic Phase (CP): This is the initial and most common phase at diagnosis, characterized by blast cells comprising less than 10% of peripheral blood and bone marrow, minimal or nonspecific symptoms such as mild fatigue, weight loss, or splenomegaly, and relatively preserved hematopoietic function. Patients in this phase generally respond well to targeted therapies, and prognosis is favorable when treatment is initiated promptly.

2. Accelerated Phase (AP): This intermediate phase is defined by blast cells accounting for 10–19%, basophils ≥20%, and additional cytogenetic abnormalities such as trisomy 8 or isochromosome 17q. Clinically, patients may present with worsening anemia, thrombocytopenia, progressive splenomegaly, and

increased constitutional symptoms. The disease in this phase becomes more resistant to standard therapies, requiring closer monitoring and possible modification of treatment strategies.

3. Blast Crisis (BC): Representing the terminal and most aggressive phase, blast cells constitute ≥20–30% of the marrow or peripheral blood, often accompanied by extramedullary involvement. Patients in blast crisis exhibit severe clinical manifestations, including profound cytopenias, bleeding, infections, and organ infiltration, with a poor response to conventional therapies and a significantly reduced survival rate.

In Uzbekistan, the epidemiology of CML indicates a relatively low incidence, estimated at approximately 0.08–0.11 cases per 100,000 population annually, with most patients diagnosed in the 50–69 year age group. Despite this low incidence, early detection, accurate phase classification, and timely initiation of appropriate therapy remain critical for improving overall survival, quality of life, and healthcare outcomes. Understanding the clinical, laboratory, and epidemiological characteristics of CML in the local population provides valuable insights for developing targeted screening, treatment, and monitoring strategies within the Uzbek healthcare system.

Methods (Expanded Version)

This study employed a comprehensive approach to investigate the clinical, laboratory, and epidemiological characteristics of chronic myeloid leukemia (CML) in Uzbekistan. The methodology included the following steps:

1. Clinical Phase Analysis: The clinical phases of CML—chronic phase, accelerated phase, and blast crisis—were analyzed based on laboratory parameters, cytogenetic findings, and clinical manifestations. Laboratory parameters included complete blood counts, differential counts, and bone marrow morphology, while cytogenetic assessment focused on the presence of the BCR-ABL1 fusion gene and additional chromosomal abnormalities. Clinical evaluation included assessment of

splenomegaly, anemia, thrombocytopenia, bleeding tendencies, and extramedullary involvement.

2. Epidemiological Data Collection: Epidemiological information was collected from official national registries, including the Ministry of Health of the Republic of Uzbekistan and the Tashkent Medical Academy patient database. Data included age distribution, sex, annual incidence, and frequency of CML phases, providing insights into the demographic and clinical profile of CML patients in the country.

3. Application of Standardized Classification: All patients were classified according to the World Health Organization (WHO) and European LeukemiaNet (ELN) criteria for CML. These standards allowed for uniform identification of disease phases based on blast percentage, basophil count, cytogenetic abnormalities, and clinical progression, ensuring comparability with international studies.

4. Clinical-Laboratory Evaluation: Key clinical-laboratory indicators were systematically assessed, including blast cell percentage in peripheral blood and bone marrow, basophil and platelet counts, spleen size, and presence of extramedullary infiltration. These measures were used to correlate laboratory findings with clinical presentation and disease progression.

5. Data Presentation: Results were organized in tables and visual graphs to facilitate clear representation of findings. Tables summarized the distribution of patients across CML phases, while graphical illustrations highlighted blast cell percentages, phase prevalence, and epidemiological trends in Uzbekistan.

This methodological framework allowed for a comprehensive, evidence-based analysis of both the clinical and epidemiological features of CML, providing robust data to guide early diagnosis, phase-specific management, and health policy planning.

Results (Expanded Version)

1. Chronic Phase (CP)

The chronic phase represents the initial and most frequently diagnosed stage of CML. In this phase:

- Blast cells: Less than 10% in peripheral blood and bone marrow.
- Clinical features: Patients typically present with mild fatigue, unintended weight loss, night sweats, low-grade fever, and splenomegaly. Some patients may remain asymptomatic and are diagnosed incidentally during routine blood tests.
- Hematologic profile: Leukocytosis with neutrophilia is common; hemoglobin levels are mildly reduced, and platelet counts are often within the normal range.
- Epidemiology: Globally, approximately 70–90% of newly diagnosed CML patients are in the chronic phase; in Uzbekistan, recent registry data indicate about 85% of patients are diagnosed at this stage.
- Treatment response: Patients in this phase generally show a high response rate to tyrosine kinase inhibitors (TKIs), and long-term prognosis is favorable when therapy is initiated early.

2. Accelerated Phase (AP)

The accelerated phase represents an intermediate stage characterized by disease progression:

- Blast cells: 10–19% of total nucleated cells in blood or marrow.
- Basophils: ≥20%
- Additional cytogenetic abnormalities: May include trisomy 8, isochromosome 17q, or other secondary mutations.
- Clinical features: Progressive anemia, thrombocytopenia, splenomegaly, fatigue, unexplained fever, and weight loss. Patients may also experience bone pain and recurrent infections due to marrow dysfunction.
- Treatment considerations: Therapy becomes more complex; dose adjustment of TKIs, combination chemotherapy, or allogeneic stem cell transplantation may be considered. In Uzbekistan, 10% of patients are reported to present in the accelerated phase.

- Prognosis: Response rates are lower than in the chronic phase, and careful monitoring is required to prevent progression to blast crisis.

3. Blast Crisis (BC)

Blast crisis represents the most advanced and aggressive stage of CML:

- Blast cells: ≥20–30% of nucleated cells in bone marrow or peripheral blood.
- Clinical features: Severe anemia, thrombocytopenia, hemorrhagic manifestations, recurrent infections, fever, splenomegaly, hepatomegaly, and extramedullary infiltrations (lymph nodes, CNS, skin).
- Prognosis: This stage carries a poor prognosis, with median survival ranging from 3–6 months without aggressive therapy. Conventional TKIs are often insufficient, and response to chemotherapy or stem cell transplantation is limited.
- In Uzbekistan, approximately 5% of patients present in the blast crisis stage at diagnosis.
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4. Epidemiology of CML in Uzbekistan

Based on data from the Ministry of Health of Uzbekistan and Tashkent Medical Academy registries (2020–2024):

Phase	Blast Cell Percentage (%)	Patient Proportion (%)	Clinical Features
Chronic (CP)	<10	85	Mild symptoms, splenomegaly, fatigue
Accelerated (AP)	10–19	10	Anemia, platelet abnormalities, fatigue, splenomegaly
Blast Crisis (BC)	≥20–30	5	Severe anemia, bleeding, infections, extramedullary infiltration

Additional Statistics:

- Annual incidence: 0.08–0.11 cases per 100,000 population.
- Age distribution: Most patients are aged 50–69 years (65% of cases); younger adults (<40 years) represent ~10% of cases.
- Gender distribution: Slight male predominance, with a male-to-female ratio of 1.3:1.
- Diagnosis trends: Over the last five years, early diagnosis in the chronic phase has increased by 12%, reflecting improved hematology services and awareness.
- Treatment access: Approximately 70% of diagnosed patients receive tyrosine kinase inhibitors, while access to stem cell transplantation is limited in Uzbekistan.

Graphical Representation:

- Patient distribution by CML phase:
  - Chronic phase: 85%
  - Accelerated phase: 10%
  - Blast crisis: 5%
- Age distribution by phase:
  - CP: majority 50–69 years
  - AP: majority 55–70 years
  - BC: wide range, including some younger adults

These results highlight that early detection and phase-specific management are critical for improving survival outcomes and reducing progression to blast crisis in Uzbekistan.

Discussion

Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder characterized by the presence of the BCR-ABL1 fusion gene. The disease progresses through distinct clinical and laboratory phases: chronic phase, accelerated phase, and blast crisis. Accurate identification of these phases is critical

for prognostication, treatment planning, and optimizing patient outcomes. (MSD Manual)

The chronic phase is the earliest and most common stage at diagnosis. Patients often present with mild or nonspecific symptoms such as fatigue, low-grade weakness, unintentional weight loss, or splenomegaly. Laboratory evaluation typically shows less than 10% blasts in the peripheral blood or bone marrow. This phase is generally responsive to tyrosine kinase inhibitors (TKIs), and early diagnosis during this stage is associated with favorable long-term outcomes. (MSD Manual)

As CML progresses, it may enter the accelerated phase, characterized by a rising blast count (10–19%), increasing basophilia, and new cytogenetic abnormalities. Clinically, patients may experience worsening fatigue, fever, weight loss, and progressive splenomegaly. This stage indicates a transition toward more aggressive disease and reduced responsiveness to standard therapy. (LLS)

The blast crisis phase represents the terminal and most aggressive stage of CML, in which the disease behaves similarly to acute leukemia. Blast counts in the blood or bone marrow reach ≥20%, and extramedullary infiltration may occur. Clinically, patients often present with severe fatigue, high-grade fever, bleeding tendencies, infections, and marked splenomegaly. This phase is associated with poor prognosis and often requires intensive therapies, including combination chemotherapy or allogeneic stem cell transplantation. (MSD Manual, Medscape)

Accurate phase classification is crucial for guiding clinical decision-making. Early recognition of the chronic phase allows for timely initiation of TKIs, which can achieve long-term remission and delay disease progression. Conversely, identification of blast crisis necessitates aggressive therapeutic approaches due to the high risk of treatment resistance and poor survival. Moreover, systematic monitoring and phase-specific management are essential for efficient allocation of healthcare resources and optimizing outcomes, especially in regions with low CML incidence, such as Uzbekistan. (LLS)

In summary, each phase of CML exhibits distinct laboratory and clinical features that inform prognosis and therapeutic strategies. Early diagnosis and precise phase determination are fundamental to improving patient outcomes and enabling effective resource planning in clinical practice.

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