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Sumathi Publications
Case Series

Chronic myeloid leukemia in adolescents and young adults: clinicopathological features and outcomes: a case series from a tertiary care institute

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Abstract

Significant advances have been made in the treatment of leukemia over the past two decades. However, the majority of research has concentrated on pediatric and elderly populations, leaving adolescents and young adults, conventionally defined as individuals aged 15–39 years, comparatively underexplored. These demographic faces unique biological, psychosocial, and therapeutic challenge that necessitate tailored management strategies. Despite transformative advances in chronic myeloid leukemia (CML) therapy through tyrosine kinase inhibitors (TKIs), studies specifically focused on adolescents and young adults' patients remain limited. A retrospective case series of eight patients aged 16–35 years presenting to the outpatient and inpatient departments of Era University, Lucknow, was conducted. All patients underwent complete blood count with differential leukocyte count, ultrasonography, bone marrow aspiration (BMA), conventional karyotyping, and reverse transcriptase–quantitative polymerase chain reaction (RT-qPCR) for BCR-ABL1 transcript quantification. All eight patients were confirmed to have CML in the chronic phase (CML-CP), with female preponderance (5:3). Prominent clinicopathological features included marked leukocytosis (TLC range: 70,000–3,00,000/µL), anemia, hepatosplenomegaly, and a left-shifted myeloid differential with elevated myeloid-to-erythroid (M:E) ratios (range: 14:1–32:1) on BMA. Philadelphia chromosome positivity and BCR-ABL1 p210 fusion transcript were confirmed in all cases by karyotyping and RT-qPCR, respectively. CML in the adolescents and young adult's population presents with distinctive clinicopathological features, including greater disease burden at diagnosis compared with older cohorts. A comprehensive understanding of prognostic determinants, treatment adherence challenges, and long-term outcomes in this age group is imperative to optimize therapeutic strategies and improve prognosis.

KEYWORDS: Chronic myeloid leukemia; Adolescents and young adults; BCR-ABL1; Philadelphia chromosome; Tyrosine kinase inhibitors; Bone marrow aspiration; Myeloproliferative neoplasm.

Introduction

Chronic myeloid leukemia (CML) is a clonal myeloproliferative neoplasm originating from a pluripotent hematopoietic stem cell and characterized by the dysregulated, excessive proliferation of the myeloid lineage with preserved differentiation capacity. The hallmark molecular event is the t (9;22) (q34;q11.2) translocation, generating the Philadelphia (Ph) chromosome and the BCR-ABL1 oncogene, which encodes a constitutively active tyrosine kinase responsible for uncontrolled granulopoiesis [1,2].

CML predominantly affects middle-aged and older adults, with a median age of onset of approximately 60–65 years and an annual incidence of 1–2 cases per 100,000 populations globally [3]. In the pediatric population, CML is exceedingly rare, accounting for only approximately 3% of all childhood leukemias [4, 5]. Adolescents and young adults (AYA), conventionally defined as those aged 15–39 years, constitute approximately 22.1% of all CML cases worldwide and account for approximately 1 million new cancer diagnoses annually within this age bracket [4,6].

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Despite this non-trivial burden, AYA patients with CML remain a relatively understudied population. The preponderance of published literature has historically focused on middle-aged or elderly cohorts, and outcomes data specific to AYA patients are sparse [7]. Available evidence suggests that AYA patients may exhibit distinct clinicopathological characteristics—including greater disease burden at presentation—and that their therapeutic responses and event-free survival may differ from those of older adults [8-10]. In India, age-specific incidence rates reported by Dikshit et al. (2001–2005) from Greater Mumbai were 0.04 per 100,000 in the pediatric group and 0.22 per 100,000 in the AYA group, underscoring the relative rarity of CML in younger individuals in the Indian context [11, 12].

The introduction of BCR-ABL1-targeted tyrosine kinase inhibitors (TKIs) has fundamentally altered the natural history of CML, with long-term survival rates now approaching those of the general population in responders. Nevertheless, event-free survival in AYA patients remains suboptimal compared with older cohorts, potentially reflecting differences in disease biology, metabolic pharmacokinetics, and challenges in therapeutic adherence unique to this age group [9, 11].

This case series presents eight AYA patients with CML-CP diagnosed at a tertiary care institute serving predominantly economically disadvantaged patients in Lucknow, India, with the aim of delineating their clinicopathological features, hematological profiles, and outcomes, and to contribute to the growing body of literature on this underrepresented demographic.

Materials and Methods

Study Design and Setting: This was a retrospective, descriptive case series conducted in the Hematology Section of the Department of Pathology, Era University (Era Lucknow Medical College & Hospital), Lucknow, Uttar Pradesh, India. The study period encompassed cases diagnosed over a defined interval. The institution serves as a major tertiary referral center for a predominantly low-income and minority patient population.

Inclusion Criteria: (i) Patients aged 16–39 years of either sex who presented to the outpatient or inpatient departments. (ii) Patients with clinical symptoms consistent with a hematological malignancy, including fever, weakness, abdominal pain, or organomegaly, who were subsequently confirmed to have CML, as well as patients with a prior diagnosis of Ph chromosome- and BCR-ABL1 fusion gene-positive CML.

Exclusion Criteria: (i) Patients older than 39 years. (ii) Patients with a confirmed diagnosis of CML who were receiving cytotoxic or TKI therapy at the time of evaluation and had already achieved haematological or molecular remission. (iii) Patients with concurrent myelosclerotic or primary myelofibrotic disorders.

Diagnostic Investigations : All suspected cases underwent a standardized diagnostic workup comprising: (i) complete blood count (CBC) with manual differential leukocyte count (DLC) on peripheral blood smear examination; (ii) abdominal ultrasonography for hepatosplenomegaly and lymphadenopathy; (iii) bone marrow aspiration (BMA) with Giemsa-stained smear morphology; (iv) conventional G-banded karyotyping for Philadelphia chromosome detection; and (v) reverse transcriptase–quantitative polymerase chain reaction (RT-qPCR) for BCR-ABL1 transcript quantification (p210 and p190 isoforms). Immunophenotyping by flow cytometry was performed in cases where blasts were identified on peripheral blood smear or **BMA**.

Results

Patient Characteristics and Investigations

All patients with suspected leukemia underwent a comprehensive diagnostic workup including CBC with manual DLC on Leishman-stained peripheral blood smears, abdominal ultrasonography, and bone marrow aspiration with Giemsa-stained morphological assessment, conventional karyotyping, and RT-qPCR for BCR-ABL1 transcript quantification. Immunophenotyping by multicolor flow cytometry was performed in cases where blasts were identified on the peripheral blood smear or BMA.

Bone Marrow Aspiration Findings: The individual BMA morphological findings for each patient are detailed below.

Case 1: BMA smears demonstrated marked hypercellularity with predominantly myeloid hyperplasia. Myeloblasts accounted for less than 2% of the myeloid precursor population, consistent with the chronic phase. Erythropoiesis was normoblastic in maturation sequence but markedly suppressed owing to the expansion of the granulocytic series, yielding an elevated myeloid-to-erythroid (M:E) ratio of 29:1. Megakaryocytes were numerous and morphologically normal, with active platelet budding. Scattered plasma cells and lymphocytes were also observed. These findings correlated with the peripheral blood smear morphology, confirming CML in the chronic phase.

Case 2: BMA smears showed hypercellularity with predominant myeloid expansion. Erythropoiesis was suppressed but maintained a normal maturation sequence, resulting in a M:E ratio of 24:1. Myeloblasts and promyelocytes together comprised approximately 3% of the myeloid series,

Table 1. Demographic data, clinical presentations, physical examination findings, hematological investigations, disease phase, and molecular results for patients included in the series with CML-CP

Case No.	Age (Y)	Sex	Disease Duration	Clinical Symptoms	CBC Findings	Phase	BCR-ABL1
1	17	F	2 yrs	Weakness, Dysmenorrhea Watery vaginal discharge, Abdominal Examination / Signs, Hepatomegaly Splenomegaly, Lung: parenchymal consolidation, Dysmenorrhea, Watery vaginal discharge, Abdominal, Examination / Signs, Hepatomegaly, Splenomegaly, Lung: parenchymal consolidation	Hb:12.3 g/dL TLC: 1.2×10^5/μL DLC — Poly: 26%, Lympho: 4%, Eosino: 5%, Mono: 2%, Baso: 2%, Blasts: 2%, Promyelo: 4%, Myelo: 30%, Metamyelo: 5%, Bands: 20%; Platelets: 2.2×10^5/μL	Chronic Phase	Positive
2	20	M	1.5 yrs	Fever Weakness Abdominal Examination / Signs Hepatomegaly Splenomegaly Lung abscess	Hb: 4.3 g/dL; TLC: 85,000/μL; DLC — Poly: 30%, Lympho: 3%, Mono: 1%, Baso: 4%, Blasts: 3%, Promyelo: 3%, Myelo: 22%, Metamyelo: 14%, Bands: 20%; Platelets: 20,000/μL	Chronic Phase	Positive
3	30	F	3 yrs	Fever, Weakness Vomiting , Abdominal pain, Weight loss Abdominal Examination / Signs Hepatomegaly Splenomegaly Lymphadenopathy	Hb: 9.5 g/dL; TLC: 1.3×10^5/ μL; DLC — Poly: 34%, Lympho: 2%, Eosino: 1%, Baso: 9%, Blasts: 2%, Promyelo: 5%, Myelo: 20%, Metamyelo: 15%, Bands: 12%; Platelets: 3.5×10^5/μL	Chronic Phase	Positive
4	29	F	2 yrs	Fatigue, Anorexia Nausea, Weight loss Abdominal fullness Limb pain Abdominal Examination / Signs Hepatomegaly Splenomegaly Lymphadenopathy	Hb: 8.7 g/dL; TLC: 1.0×10^5/μL DLC — Poly: 33%, Lympho: 4%, Eosino: 6%, Baso: 3%, Blasts: 2%, Promyelo: 4%, Myelo: 32%, Metamyelo: 8%, Bands: 8%; Platelets: 4.8×10^5/μL	Chronic Phase	Positive
5	27	F	2.5 yrs	Fever, Weakness Nausea, Weight loss Abdominal fullness/bloating Abdominal pain Abdominal Examination / Signs Hepatomegaly Splenomegaly Lymphadenopathy	Hb: 7.5 g/dL; TLC: 1.5×10^5/μL; DLC — Poly: 20%, Lympho: 2%, Eosino: 5%, Baso: 8%, Blasts: 2%, Promyelo: 15%, Myelo: 26%, Metamyelo: 14%, Bands: 8%; Platelets: 1.5×10^5/μL	Chronic Phase	Positive
6	30	M	1 yr	Fever Limb pain Abdominal Examination / Signs Hepatomegaly Splenomegaly Pleural effusion	Hb: 11.0 g/dL; TLC: 70,000/μL; DLC — Poly: 20%, Lympho: 2%, Eosino: 6%, Baso: 4%, Blasts: 2%, Promyelo: 22%, Myelo: 24%, Metamyelo: 10%, Bands: 8%; Platelets: 2.4×10^5/μL	Chronic Phase	Positive
7	22	M	5 yrs	Fever, Weakness Abdominal fullness Heartburn, Limb pain Abdominal Examination / Signs Hepatomegaly Splenomegaly Lymphadenopathy	Hb: 10.7 g/dL; TLC: 1.2×10^5/μL; DLC — Poly: 35%, Lympho: 7%, Eosino: 3%, Mono: 1%, Baso: 5%, Blasts: 4%, Promyelo: 12%, Myelo: 20%, Metamyelo: 5%, Bands:8%; Platelets: 2.0×10^5/μL	Chronic Phase	Positive
8	28	F	3 yrs	High fever Weakness Severe abdominal pain Weight loss Abdominal Examination / Signs Hepatomegaly Splenomegaly Lymphadenopathy	Hb: 8.1 g/dL; TLC: 3.0×10^5/μL; DLC Poly: 30%, Lympho: 2%, Eosino: 2%, Mono: 0%, Baso: 8%, Blasts: 2%, Promyelo: 10%, Myelo: 26%, Metamyelo: 12%, Bands: 8%; Platelets: 3.8×10^5/μL	Chronic Phase	Positive

TLC = total leukocyte count; DLC = differential leukocyte count; Hb = hemoglobin; Poly = polymorphonuclear neutrophils; Lympho = lymphocytes; Eosino = eosinophils; Mono = monocytes; Baso = basophils; Promyelo = promyelocytes; Myelo = myelocytes; Metamyelo = metamyelocytes; Bands = band forms.

effectively excluding blast crisis. Basophilic myelocytes and metamyelocytes were present but insufficient in quantity to fulfill criteria for the accelerated phase. Megakaryocytes were morphologically normal. Peripheral blood smear and BMA findings were concordant, supporting a diagnosis of CML-CP.

Case 3: Hypercellular marrow with marked expansion of the mid-myeloid compartment was observed. Erythropoiesis was suppressed despite a preserved normal maturation sequence, producing a M:E ratio of 14:1. Myeloblasts and promyelocytes collectively constituted approximately 5% of the myeloid precursors. Basophil precursors were increased above the reference range but did not meet criteria for the accelerated phase. The megakaryocytic lineage demonstrated mild hyperplasia with morphologically normal forms. Findings were consistent with CML-CP on correlation with the peripheral blood smear.

Case 4: Hypercellular marrow with prominent myeloid hyperplasia was noted. Despite markedly increased myelopoiesis, erythroid maturation remained morphologically normal, with an elevated M:E ratio of 20:1. Myeloblasts and promyelocytes constituted approximately 3% of the nucleated cell population, excluding blast crisis. Band cells, metamyelocytes, and myelocytes were abundant. Basophil precursors exceeded the normal range but were insufficient to support a diagnosis of accelerated phase. Morphologically normal megakaryocytes demonstrated active platelet formation. Aspiration findings correlated with the peripheral blood smear, consistent with CML-CP.

Case 5: Marked hypercellularity with predominantly myeloid hyperplasia was identified. Erythropoiesis was suppressed but maturationally intact, yielding a M:E ratio of 19:1. Myeloblasts and promyelocytes comprised approximately 3% of the myeloid series. Band forms, metamyelocytes, and myelocytes were numerous. Although basophil precursors were elevated, the degree did not meet accelerated phase criteria. Mild megakaryocytic hyperplasia with morphologically normal forms was observed. These findings were consistent with the peripheral blood smear, confirming CML in the chronic phase.

Case 6: BMA demonstrated hypercellularity with a predominance of myeloid precursors. Myeloblasts accounted for less than 2% of total myeloid cells. Erythropoiesis was present with a normal maturation sequence, and the M:E ratio was markedly elevated at 32:1. Morphologically normal megakaryocytes were actively producing platelets. Plasma cells, lymphocytes, and eosinophils were also noted. These morphological features, in conjunction with the peripheral blood smear findings, were consistent with a myeloproliferative neoplasm (MPN), subsequently confirmed as CML-CP by cytogenetic and molecular studies.

Case 7: Hypercellular marrow with predominantly myeloid hyperplasia was seen. Erythropoiesis was suppressed but preserved in maturation sequence, with a M:E ratio of 23:1. Myeloblasts constituted less than 5% of nucleated cells. The overall morphological pattern was consistent with CML-CP, corroborated by peripheral blood smear correlation.

Case 8: A hypercellular BMA with predominantly myeloid hyperplasia was observed. Erythropoiesis was suppressed with a preserved normal maturation sequence, and the M:E ratio was 21:1. Promyelocytes and myeloblasts collectively accounted for approximately 3% of nucleated cells. Basophil precursors were numerous but below accelerated phase thresholds. Mild megakaryocytic hyperplasia was present, with morphologically normal forms actively forming platelets. These findings were concordant with the peripheral blood smear, consistent with a myeloproliferative neoplasm, confirmed as CML-CP (fig 4)

Cytogenetic and Molecular Findings: Conventional G-banded karyotyping confirmed the presence of the Philadelphia chromosome [t(9;22)(q34;q11.2)] in all eight cases. RT-qPCR for BCR-ABL1 transcript quantification demonstrated expression of the p210 (e14a2 or e13a2) fusion transcript in all eight patients, with BCR-ABL1/ABL1 ratios exceeding 66% in each case, indicating a high disease burden at diagnosis.

Key Findings: Among the eight cases, female patients predominated (n = 5; 62.5%). The age range was 17–30 years (mean: 25.5 years). Disease duration at presentation ranged from 1 to 5 years. All patients presented with hepatosplenomegaly; lymphadenopathy was present in five cases (62.5%). Pulmonary involvement (parenchymal consolidation, pleural effusion, or lung abscess) was observed in three cases (37.5%). Hemoglobin levels ranged from 4.3 to 12.3 g/dL (mean: 9.0 g/dL), reflecting variable degrees of anemia. TLC ranged from 70,000 to 3,00,000/µL. All cases were confirmed as CML in the chronic phase.

Illustrative Morphology

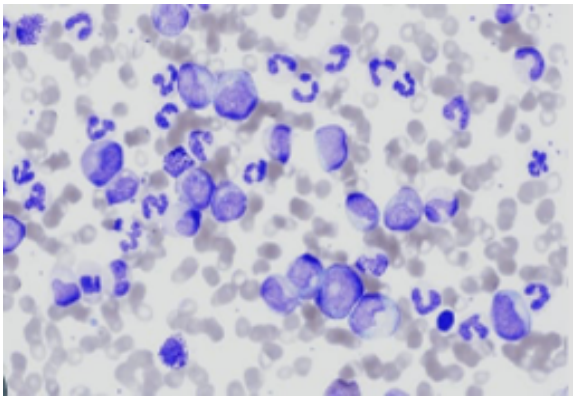

Fig 1. Peripheral blood smear: CML, Chronic Phase (10×). Left-shifted granulocytic series with myelocytes, metamyelocytes, and band forms on a background of marked leukocytosis.

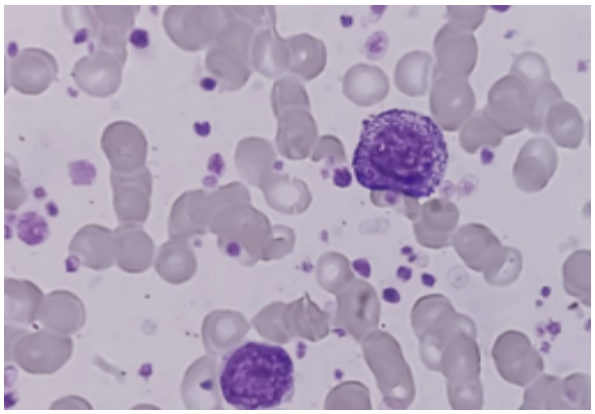

Fig 2. Peripheral blood smear: CML, Accelerated Phase (40×). Increased proportion of blasts and promyelocytes with prominent basophilia

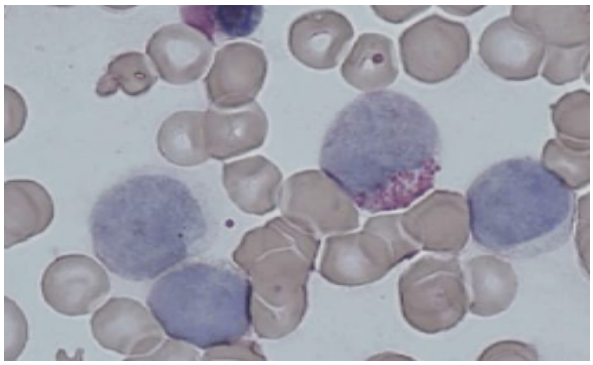

Fig 3. Peripheral blood smears: Blast Crisis (100×, oil immersion). Predominance of blasts (≥20%) with loss of normal myeloid maturation

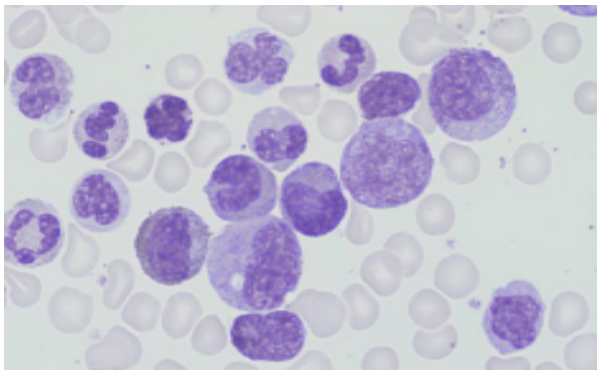

Fig 4. Bone marrows aspirate (100×, oil immersion). Marked myeloid hyperplasia with hypercellularity, suppressed erythropoiesis, and elevated M:E ratio, consistent with CML-CP

Discussion

CML has traditionally been regarded as a disease of middle-aged and older adults; however, accumulating evidence indicates that adolescents and young adults are a clinically distinct and underrepresented cohort with unique disease characteristics and therapeutic challenges [4, 8, 11]. The present case series, derived from an institution primarily serving economically disadvantaged patients in northern India, corroborates several observations from the published literature while contributing additional insights relevant to the AYA demographic in low-resource settings.

The molecular pathogenesis of CML is driven by the BCR-ABL1 oncoprotein, which constitutively activates multiple downstream signaling cascades—including the RAS/MAPK, JAK-STAT, and PI3K/AKT pathways—resulting in uncontrolled myeloid proliferation, inhibition of apoptosis, and impaired adhesion of progenitor cells to the bone marrow stroma [1, 2, 13]. The clinical and hematological sequelae observed in our patients, including marked leukocytosis, anemia, and hepatosplenomegaly, directly reflect the pathophysiology of deregulated hematopoiesis.

In the present series, female patients predominated (62.5%), a finding somewhat divergent from the reported male preponderance in most global CML cohorts. This observation may reflect referral patterns or socioeconomic factors that influence health-seeking behavior at this institution. The mean age at presentation was 25.5 years, consistent with the AYA definition. Notably, five of eight patients (62.5%) had a disease duration exceeding one year prior to confirmed diagnosis, highlighting the diagnostic delays that are characteristic of resource-limited settings and may partly account for the higher disease burden at presentation [6, 8].

All eight patients presented with hepatosplenomegaly; splenomegaly is a cardinal feature of CML-CP and correlates with the degree of myeloid expansion and extramedullary hematopoiesis [14]. Symptom burden was substantial across the cohort and included constitutional symptoms such as fever, weight loss, fatigue, and abdominal discomfort attributable to splenic and hepatic enlargement. Pulmonary involvement, in the form of parenchymal consolidation, pleural effusion, or lung abscess, was documented in three patients (37.5%), reflecting either CML-related infiltration or complicating opportunistic infection secondary to immune dysregulation—a finding that warrants further clinical scrutiny in future studies [11, 15].

Hematological parameters demonstrated the classic leukocytosis of CML-CP. Hemoglobin levels were markedly reduced in several cases (minimum: 4.3 g/dL in Case 2), reflecting suppressed erythropoiesis consequent to myeloid expansion. Basophilia was consistently identified across cases and is a diagnostically important feature of CML-CP; basophilia exceeding 20% on the peripheral blood smear is a defining criterion for the accelerated phase, a threshold not met in any of the eight patients [16]. Peripheral blood smear examination uniformly revealed a left-shifted granulocytic series with myelocytes, metamyelocytes, and band forms, accompanied

by eosinophilia and basophilia—the hallmark morphological signature of CML-CP [1].

BMA findings were concordant with peripheral blood morphology in all cases. Hypercellular marrow with marked myeloid hyperplasia, suppressed erythropoiesis, and elevated M:E ratios (range: 14:1–32:1) were universal. Myeloblast percentages remained below 10% in all cases, consistent with the chronic phase [16, 17]. The megakaryocytic lineage demonstrated normal morphology with active platelet production across all cases, a feature that distinguishes CML-CP from myelofibrosis and other myeloproliferative neoplasms [17].

Cytogenetic analysis confirmed the Philadelphia chromosome in all eight patients, and RT-qPCR demonstrated the BCR-ABL1 p210 transcript—the predominant molecular form in adult-onset CML—in all cases, with transcript burdens exceeding 66%. These molecular findings are concordant with established diagnostic criteria for CML-CP [16, 17].

Disease Phases and Diagnostic Criteria

For the purpose of this review, the diagnostic criteria for each phase of CML are briefly outlined:

Chronic Phase (CP): Peripheral blood leukocytosis (TLC typically 70,000–1,20,000/μL in adults; up to 2,50,000/μL in children), with a characteristic left-shifted granulocytic differential comprising myelocytes, metamyelocytes, band forms, and segmented neutrophils. Blasts constitute less than 10% of peripheral blood or BMA nucleated cells. Constitutional symptoms (abdominal discomfort, fatigue, weight loss, night sweats) and physical findings of pallor, mild pyrexia, and hepatosplenomegaly are common. Platelet count is generally within the normal range or elevated; significant thrombocytopenia is unusual. Splenomegaly is strongly associated with higher WBC counts (fig 1) [17, 18].

Accelerated Phase (AP): Defined by one or more of the following: (i) persistent or increasing leukocytosis (>100,000/μL) refractory to therapy; (ii) treatment-refractory splenomegaly; (iii) thrombocytosis (>1,00,000/μL) or thrombocytopenia (<1,00,000/μL) unrelated to therapy; (iv) acquisition of additional cytogenetic abnormalities (clonal evolution); (v) basophilia ≥20% in the peripheral blood; or (vi) blasts comprising 10–19% of nucleated cells in peripheral blood or BMA (fig 2) [14, 16].

Blast Phase (BP) / Blast Crisis: Defined by ≥20% blasts in the peripheral blood or bone marrow, or the presence of extramedullary blast proliferation [16]. Blast crisis confers a markedly adverse prognosis, with median survival of approximately 3–9 months. Morphologically, blast crisis is most commonly myeloid (60–70%) but may be lymphoblastic (predominantly B-lymphoid precursor; ~30%) or of mixed lineage [17, 18]. The presence of p53 mutations in late chronic phase has been associated with genomic instability and heightened risk of transformation to blast crisis [21, 22].

Treatment Considerations in AYA Patients (fig 3)

The advent of BCR-ABL1-targeted TKI therapy—beginning with imatinib (first-generation) and followed by dasatinib and nilotinib (second-generation) and bosutinib and ponatinib (third-generation)—has fundamentally transformed the management of CML, with 10-year overall survival rates exceeding 80% in CML-CP [9, 15]. Imatinib remains a preferred frontline agent given its established long-term safety profile, efficacy, and cost-effectiveness, particularly relevant in resource-limited settings.

Second-generation TKIs (dasatinib, nilotinib) achieve deeper and more rapid molecular responses compared with imatinib, particularly in terms of major molecular response (MMR) and deep molecular response (DMR) at MR^4 and $MR^{4.5}$ levels, which are prerequisite for treatment-free remission (TFR) [15]. In younger patients, the prospect of TFR is particularly clinically meaningful given the long life expectancy and desire to discontinue indefinite therapy, including for fertility and quality-of-life considerations. Accordingly, second-generation TKIs may be preferentially considered in AYA patients who can tolerate and adhere to therapy [15].

Nevertheless, published evidence consistently demonstrates that AYA patients with CML exhibit comparatively inferior TKI responses relative to older adults—a paradox given the expectation of greater physiological reserve [11, 23]. Pemmaraju et al. (2012) reported that AYA patients demonstrated lower rates of complete cytogenetic response and major molecular response compared with older cohorts treated with frontline TKI therapy [23]. Castagnetti et al. (2015) similarly identified differences in molecular response kinetics across age groups [11]. The mechanistic basis for these disparities likely reflects a combination of intrinsic disease biology, altered drug pharmacokinetics and bioavailability in younger patients, and challenges specific to the AYA cohort regarding treatment adherence—factors including competing life priorities, psychosocial stressors, financial barriers, and limited access to specialized multidisciplinary care [11, 23].

In CML-CP, TKI therapy is superior to allogeneic stem cell transplantation (allo-SCT) as initial therapy, reserving allo-SCT for patients with TKI failure, intolerance, or progression to accelerated

or blast phase. Decision-making regarding TKI selection should be individualized, accounting for patient comorbidities, fertility considerations, Ph-positive variant karyotypes, BCR-ABL1 transcript type, and baseline Sokal or ELTS risk score [9, 16].

In the context of our study cohort, all patients were from low-income strata with limited access to second-generation TKIs, underscoring the critical role of socioeconomic determinants in CML management outcomes in developing-country settings. This observation emphasizes the urgent need for improved access to affordable TKI therapy and specialized AYA oncology services in India and similar settings.

Conclusion

This retrospective case series documents eight AYA patients with CML-CP from a tertiary care institution in northern India, characterized by a female predominance, significant diagnostic delay, high disease burden at presentation, and universal BCR-ABL1 p210 fusion transcript positivity. The clinicopathological features of our cohort—including marked leukocytosis, hepatosplenomegaly, myeloid hyperplasia with elevated M:E ratios on BMA, and constitutional symptomatology—are consistent with, and extend, the existing literature on CML in the AYA population.

Critically, three of eight patients were previously undiagnosed at presentation and were identified through systematic clinical and laboratory evaluation, emphasizing the importance of maintaining a high index of clinical suspicion for CML in younger patients presenting with unexplained leukocytosis and organomegaly.

There remains a substantial paucity of evidence regarding the optimal prognostic stratification, therapeutic sequencing, and long-term outcomes of CML in AYA patients, particularly in the context of low-resource settings where access to second-generation TKIs and comprehensive psychosocial support may be limited. Future prospective, multicenter studies are needed to delineate the distinct biological and clinical determinants of CML in this cohort and to develop tailored, evidence-based management protocols that address the unique needs of AYA patients, with the overarching goal of improving disease-free and overall survival in this vulnerable population.

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Conflicts of Interest: The authors declare no conflicts of interest.

Ethical Considerations: This retrospective case series was conducted in accordance with the ethical principles of the Declaration of Helsinki. Patient data were anonymized prior to analysis. Institutional ethical approval was obtained as per institutional protocol.

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