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Original Research Article

Clinico-Pathological Profile, Treatment Patterns and Outcome of Chronic Myeloid Leukemia Patients - A Retrospective Prospective Observational Study from a Tertiary Care Center in North India

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Abstract

Introduction: Chronic myeloid leukemia (CML) is a myeloproliferative disorder characterized by the BCR-ABL1 fusion gene, resulting in uncontrolled myeloid proliferation. Tyrosine kinase inhibitors (TKIs) have transformed CML management, improving hematologic, cytogenetic, and molecular outcomes. Early treatment response and risk stratification are key predictors of long-term survival.

Aims and Objectives: This study aimed to evaluate the clinico-demographic profile, hematologic and biochemical parameters, treatment responses, adverse effects, and survival outcomes of CML patients receiving frontline TKI therapy.

Materials and Methods: A total of 307 patients were prospectively enrolled. Demographics, clinical features, laboratory parameters, and Sokal risk scores were recorded. Hematologic, cytogenetic, and molecular responses to TKI therapy were monitored, alongside adverse events. Correlation analyses were performed to assess predictors of overall survival (OS) and event-free survival (EFS).

Results: Participants were predominantly aged 21–40 years (45.93%), with slight male predominance (54.07%) and rural residence (79.48%). Fatigue (73.29%) and abdominal pain (45.73%) were common. Leukocytosis was present in 97.72%, and elevated lactate dehydrogenase in 98.05%. All achieved complete hematologic response; early molecular, cytogenetic, and major molecular responses were attained in 59.61%, 60.73%, and 66.26% at 12 months, respectively. Dyspepsia (56.25%) and thrombocytopenia (45.98%) were the most frequent adverse effects. Younger age, chronic phase, and early cytogenetic/molecular responses correlated positively with OS and EFS, while advanced phase and higher Sokal scores predicted poorer outcomes.

Conclusion: Early TKI initiation, regular monitoring, and risk stratification are essential to optimize survival and treatment outcomes in CML patients.

Keywords: Chronic Myeloid Leukemia, Tyrosine Kinase Inhibitors, Hematologic Response, Molecular Response, Survival Outcomes.

Introduction

Chronic Myeloid Leukemia (CML) is a clonal hematopoietic stem cell disorder belonging to the group of myeloproliferative neoplasms (MPNs), characterized by excessive proliferation of the myeloid lineage, particularly granulocytes, in the bone marrow and peripheral blood [1,2]. The defining molecular hallmark of CML is the Philadelphia (Ph) chromosome, a shortened derivative of chromosome 22 resulting from a reciprocal translocation between chromosomes 9 and 22, designated as t(9;22)(q34;q11), which leads to the formation of the BCR-ABL1 fusion gene [3,4]. This fusion gene encodes a constitutively active tyrosine kinase oncoprotein that drives leukemogenesis by promoting uncontrolled cell proliferation, inhibiting apoptosis, impairing differentiation, and inducing genomic instability in hematopoietic stem cells [3,4]. The presence of the

Philadelphia chromosome is diagnostic in over 95% of patients and serves as a critical target for molecular therapies [5].CML exhibits a triphasic clinical course, progressing from an indolent Chronic Phase (CP) to an Accelerated Phase (AP) and ultimately to Blast Crisis (BC) if left untreated [5,6]. The chronic phase, seen in most patients at diagnosis, is often asymptomatic or presents with nonspecific manifestations such as fatigue, weight loss, abdominal fullness from splenomegaly, and leukocytosis [6]. Laboratory findings reveal marked granulocytic proliferation with less than 10% blasts in peripheral blood or bone marrow [6]. The accelerated phase represents a transitional stage marked by increasing blast counts (10–19%), cytopenias, additional cytogenetic abnormalities, and clinical progression [7]. Blast crisis, the terminal and most aggressive phase, is characterized by ≥20% blasts, extramedullary proliferation, and rapid disease progression resembling acute leukemia, with poor prognosis and limited therapeutic response [7,8].The introduction of tyrosine kinase inhibitors (TKIs), such as Imatinib, Dasatinib, and Nilotinib, has revolutionized the management of CML by selectively inhibiting the BCR-ABL1 kinase, thereby controlling leukemic cell proliferation and improving survival outcomes [8,9]. Modern diagnostic approaches integrate complete blood counts, peripheral smears, bone marrow aspiration, cytogenetic analysis (karyotyping and FISH), and quantitative PCR for BCR-ABL1, allowing precise diagnosis, disease monitoring, and assessment of therapeutic response [9,10]. These advancements in molecular diagnostics, targeted therapy, and phase-specific management strategies have dramatically transformed the natural history of CML, enabling long-term remission and even treatment-free survival in many patients worldwide [9,10].

Materials and Methods

Study Design: The present study is a retrospective-prospective descriptive single-center study.

Place of Study: The Department of Clinical Hematology and Bone Marrow Transplant of Sher-I-Kashmir Institute of Medical Science (SKIMS) Soura.

Period of study: January 2016 to June 2025.

Study Population: All patients with a diagnosis of chronic myeloid leukemia who had already presented and who were presenting to the department during the study period were enrolled.

Sample Size: 307 Participants.

Inclusion Criteria: All consecutive diagnoses of chronic myeloid leukemia patients presenting to the department of clinical hematology, SKIMS, in the above-mentioned period.

Exclusion Criteria

- Patients not giving informed consent.
- All Philadelphia-positive ALL and AML patients.
- Patients with atypical or other myeloproliferative neoplasms.

Study Variable

- Age
- Gender
- Locale
- Laboratory Variables
- Treatment-Related Variables
- Adverse Effects
- Outcome Variables

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while Data were entered into Excel and analyzed using SPSS and GraphPad Prism.

Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result

Table 1: Distribution Mean of study patients on the basis of age group (N=307)

Variable	Groups	Mean	SD	Frequency	Percentage
Age	<20 years	16.33	3.72	18	5.86%
	21–40 years	32.07	5.89	141	45.93%
	41–60 years	49.97	5.78	108	35.18%
	>60 years	68.52	6.75	40	13.03%

Table 2: Baseline Demographic, Clinical, and Laboratory Characteristics of Study Participants (N=307)

Variable	Category	Frequency	Percentage
Gender	Males	166	54.07%
	Females	141	45.93%
Locale	Rural	244	79.48%
	Urban	63	20.52%
Fever	No	252	82.09%
	Yes	55	17.91%
Abdominal Pain	No	168	54.72%
	Yes	139	45.73%
Fatigue	No	82	26.71%
	Yes	225	73.29%
Bleeding	No	293	95.44%
	Yes	14	4.56%
Others	No	285	92.83%
	Yes	22	7.17%
Sokal Risk Group (N=307)	Low	51	16.61%
	Intermediate	176	57.33%
	High	80	26.06%
Bilirubin (N=307)	Normal	253	82.41%
	Hyperbilirubinemia	54	17.59%
Alanine Transaminase (U/L)	Normal (≤45)	283	92.18%
	Transaminitis (>45)	24	7.82%
Lactate Dehydrogenase (U/L)	Normal (140–280)	6	1.95%
	High (>280)	301	98.05%
Creatinine (mg/dL)	Normal (<1.2)	277	90.23%
	Azotemia (>1.2)	30	9.77%
Uric Acid (mg/dL)	Normal (<7)	157	51.14%
	Hyperuricemia (>7)	150	48.86%
Bone Marrow Fibrosis	Yes	4	1.30%
	No	303	98.70%

Table 3: Frequency and Percentage of Symptom Combinations and Clinical Outcomes in the Study Population

Variable	Frequency	Percentage
Abdominal Pain, Fatigue	109	52.16%
Fever, Fatigue	46	22.00%
Fever, Abdominal Pain	20	9.57%
Fever, Abdominal Pain, Fatigue	16	7.66%
Fatigue, Bleeding	11	5.26%
Fatigue, Others	6	2.87%
Bleeding, Others	1	0.48%
Event-Free Survival	250	81.50%
Event (Disease progression or Death)	57	18.50%

Table 4: Distribution of White Blood Cell, Platelet, and Basophil Counts Among Study Participants

WBC Count (µL)	Normal (4,500–11,000 cells/µL)	3	0.98%
	Leukocytosis (>11,000 cells/µL)	300	97.72%
	Leukopenia (<4,000 cells/µL)	4	1.30%
PLT Count (µL)	Thrombocytopenia (<150,000 cells/µL)	63	20.53%
	Normal (150,000–450,000 cells/µL)	180	58.63%
	Thrombocytosis (>450,000 cells/µL)	64	20.84%
Basophil Count (N=307)	<5%	10	3.26%
	>5%	297	96.74%

Table 5: Treatment Response, TKI Modification Reasons, and Adverse Effects in Chronic Myeloid Leukemia Patients

Parameter	Category	Frequency (N)	Percentage (%)
Reasons for TKI Change (N=127)	Poor response	110	86.61
	Intolerance	5	3.94
	Poor response & Intolerance	4	3.15
	Poor response & Toxicity	4	3.15
	Toxicity	3	2.36
	Poor response, Intolerance & Toxicity	1	0.79
Complete Hematologic Response (CHR) (N=307)	Yes	307	100
	No	0	0
Early Molecular Response (EMR) (N=307)	Yes	183	59.61
	No	124	40.39
Complete Cytogenetic Response (N=275)	Six Months	65	23.64
	Twelve Months	167	60.73
	Beyond Twelve Months	43	15.63
Major Molecular Response (N=243)	Six Months	40	16.46
	Twelve Months	161	66.26
	Eighteen Months	29	11.94
	Beyond Eighteen Months	13	5.34
Adverse Effects (N=224)	Dyspepsia	126	56.25
	Thrombocytopenia	103	45.98
	Anemia	57	25.45
	Neutropenia	57	25.45
	Myalgias	19	8.48
	Pleural Effusion	10	4.46
	Hepatotoxicity	7	3.12
	Nephrotoxicity	6	2.68
	Skin Rash	2	0.89

Table 6: Correlation of Baseline and Treatment Variables with Estimated Overall Survival (OS) and Event-Free Survival (EFS) in CML Patients

Variables	Age	Estimated OS	Estimated EFS
Age	1	-0.214**	-0.232**
p-value	—	<0.001)	<0.001)
N	307	307	250
Estimated OS	-	1	0.970**
p-value	—	—	<0.001)
N	—	307	307
Estimated EFS	-	-	1
Platelet Count	1	0.056	0.074
p-value	—	0.33	0.196
N	307	307	250
Estimated OS	—	1	0.970**
p-value	—	—	<0.001)
N	—	307	307
Estimated EFS	—	—	1
CCR (12M)	1	0.352*	0.362*
p-value	—	0	<0.001)
N	307	307	307
Estimated OS	—	1	0.970**
p-value	—	—	<0.001)
N	—	307	307
Estimated EFS	—	—	1
MMR (6M)	1	0.255**	0.254**
p-value	—	<0.001)	<0.001)

N	296	307	296
Estimated OS	—	1	0.970**
p-value	—	—	<0.001)
N	—	307	307
Estimated EFS	—	—	1
MMR (12M)	1	0.372**	0.374**
p-value	—	<0.001)	<0.001)
N	307	307	307
Estimated OS	—	1	0.970**
p-value	—	—	<0.001)
N	—	307	307
Estimated EFS	—	—	1
CML Phase	1	-0.197**	-0.188**
p-value	—	0.001	0.001
N	307	307	307
Estimated OS	—	1	0.970**
p-value	—	—	<0.001)
N	—	307	307
Estimated EFS	—	—	1
Frontline TKIs	1	0.016	0.036
p-value	—	0.776	0.528
N	307	307	207
Estimated OS	—	1	0.970**
p-value	—	—	<0.001)
N	—	307	307
Estimated EFS	—	—	1
Sokal Risk Groups	1	-0.175**	0.041
p-value	—	0.002	0.514
N	307	307	250
Estimated OS	—	1	0.970**
p-value	—	—	<0.001)
N	—	307	307
Estimated EFS	—	—	1

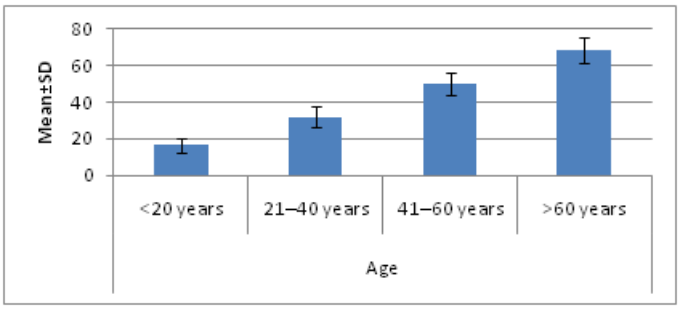

Figure 1: Distribution Mean of study patients on the basis of age group (N=307)

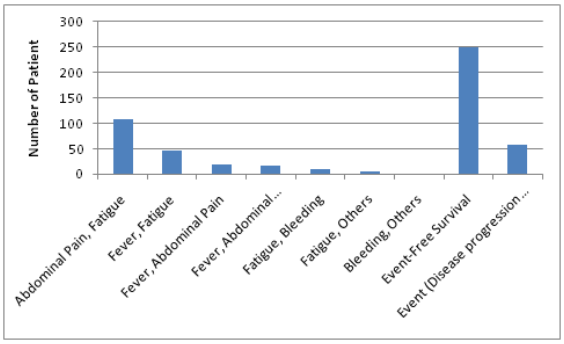

Figure 2: Frequency and Percentage of Symptom Combinations and Clinical Outcomes in the Study Population

The study included a total of 307 participants with a wide age range. The mean age of participants in the <20 years group was 16.33 ± 3.72 years, comprising 18 individuals (5.86%). The 21–40 years group constituted the largest proportion, with 141 participants (45.93%) and a mean age of 32.07 ± 5.89 years. Participants aged 41–60 years numbered 108 (35.18%) with a mean age of 49.97 ± 5.78 years, while those over 60 years included 40 individuals (13.03%) with a mean age of 68.52 ± 6.75 years. Overall, the majority of the study population belonged to the 21–40 years age group.

Out of the 307 participants, 166 (54.07%) were males and 141 (45.93%) were females. The majority resided in rural areas (244, 79.48%), while 63 (20.52%) were from urban areas. Regarding clinical features, fever was present in 55 participants (17.91%) and abdominal pain in 139 (45.73%). Fatigue was reported by 225 participants (73.29%), whereas bleeding and other symptoms were less common, observed in 14 (4.56%) and 22 (7.17%) participants, respectively. According to the Sokal risk stratification, 51 participants (16.61%) were low-risk, 176 (57.33%) intermediate-risk, and 80 (26.06%) high-risk. Laboratory investigations showed that bilirubin was elevated in 54 participants (17.59%), alanine transaminase was raised in 24 (7.82%), and lactate dehydrogenase was high in 301 participants (98.05%). Creatinine was elevated in 30 participants (9.77%), while uric acid levels were above normal in 150 participants (48.86%). Bone marrow fibrosis was present in only 4 participants (1.30%).

Among the study participants, the most common combination of symptoms was abdominal pain with fatigue, observed in 109 individuals (52.16%), followed by fever with fatigue in 46 participants (22.00%). Other symptom combinations included fever and abdominal pain in 20 participants (9.57%), fever, abdominal pain, and fatigue in 16 participants (7.66%), fatigue with bleeding in 11 participants (5.26%), fatigue with other symptoms in 6 participants (2.87%), and bleeding with other symptoms in 1 participant (0.48%). Regarding outcomes, event-free survival was observed in 250 participants (81.50%), whereas 57 participants (18.50%) experienced an event, defined as disease progression or death.

Hematological analysis revealed that the majority of participants had leukocytosis, with 300 individuals (97.72%) exhibiting WBC counts above 11,000 cells/µL, while leukopenia was observed in 4 participants (1.30%) and normal counts in 3 participants (0.98%). Platelet counts were normal in 180 participants (58.63%), whereas thrombocytopenia was present in 63 participants (20.53%) and thrombocytosis in 64 participants (20.84%). Analysis of basophil counts showed that 297 participants (96.74%) had basophils exceeding 5%, while only 10 participants (3.26%) had basophils below 5%.

Among the 127 participants who required a change in TKI therapy, the most common reason was poor response in 110 individuals (86.61%), followed by intolerance in 5 participants (3.94%). Combinations of poor response with intolerance or toxicity were less frequent, with only 4 participants (3.15%) each experiencing poor response with intolerance or poor response with toxicity. A single participant (0.79%) had all three issues—poor response, intolerance, and toxicity. All 307 participants (100%) achieved complete hematologic response (CHR), while early molecular response (EMR) was observed in 183 participants (59.61%). Regarding cytogenetic outcomes, complete cytogenetic response was achieved in 65 participants (23.64%) by six months, 167 participants (60.73%) by twelve months, and 43 participants (15.63%) beyond twelve months. Major molecular response (MMR) was seen in 40 participants (16.46%) at six months, 161 (66.26%) at twelve months, 29 (11.94%) at eighteen months, and 13 (5.34%) beyond eighteen months. Among 224 participants monitored for adverse effects, the most common was dyspepsia in 126 participants (56.25%), followed by thrombocytopenia in 103 (45.98%), anemia and neutropenia each in 57 participants (25.45%), myalgias in 19 (8.48%), pleural effusion in 10 (4.46%), hepatotoxicity in 7 (3.12%), nephrotoxicity in 6 (2.68%), and skin rash in 2 participants (0.89%).

Correlation analysis was performed to evaluate the relationship between various clinical and treatment-related variables with estimated overall survival (OS) and event-free survival (EFS). Age showed a significant negative correlation with both estimated OS ($r = -0.214$, $p < 0.001$) and EFS ($r = -0.232$, $p < 0.001$).

Complete cytogenetic response at 12 months (CCR 12M) and major molecular response at 6 and 12 months (MMR 6M, MMR 12M) were positively correlated with estimated OS ($r = 0.352$, 0.255, 0.372; all $p < 0.001$) and EFS ($r = 0.362$, 0.254, 0.374; all $p < 0.001$). CML phase was negatively correlated with OS ($r = -0.197$, $p = 0.001$) and EFS ($r = -0.188$, $p = 0.001$), while Sokal risk groups showed a weak negative correlation with OS ($r = -0.175$, $p = 0.002$) but no significant correlation with EFS ($r = 0.041$, $p = 0.514$). No significant correlations were observed for platelet count or frontline TKI type with either OS or EFS. Overall, achievement of cytogenetic and molecular responses, younger age, and chronic phase CML were associated with better survival outcomes.

Discussion

In this study of 307 participants with chronic myeloid leukemia (CML), the majority were aged

21–40 years and resided in rural areas, with a slight male predominance. Fatigue and abdominal pain were the most commonly reported symptoms, whereas bleeding and other manifestations were less frequent. Laboratory evaluation revealed a high prevalence of leukocytosis and elevated lactate dehydrogenase levels, reflecting the proliferative nature of CML at diagnosis. These demographic and baseline clinical characteristics are in line with previous studies, which also reported higher CML incidence among young to middle-aged adults, predominantly males [11–13]. All participants achieved complete hematologic response (CHR), and a majority attained early molecular response (EMR) and complete cytogenetic response (CCR) within 12 months, while major molecular response (MMR) was most commonly achieved at 12 months. These treatment outcomes are consistent with prior reports demonstrating high hematologic and molecular response rates with frontline tyrosine kinase inhibitors in chronic phase CML [14–16]. Adverse effects were generally manageable, with dyspepsia and thrombocytopenia being the most common, similar to previously documented safety profiles [17–18]. Correlation analysis indicated that younger age, achievement of cytogenetic and molecular responses, and chronic phase at diagnosis were associated with better overall survival (OS) and event-free survival (EFS), whereas advanced phase and higher Sokal risk scores predicted poorer outcomes. These findings corroborate earlier studies highlighting the prognostic significance of early molecular and cytogenetic responses in predicting long-term survival in CML [19–20]. Overall, our study reinforces the importance of early TKI therapy, regular monitoring of hematologic and molecular responses, and risk stratification in optimizing clinical outcomes in patients with CML.

Conclusion

In conclusion, this study highlights that chronic myeloid leukemia predominantly affects young to middle-aged adults, with fatigue and abdominal pain being the most common clinical features. Most patients respond well to frontline tyrosine kinase inhibitor therapy, achieving favorable hematologic, cytogenetic, and molecular responses, while adverse effects remain generally manageable. Younger age, chronic phase at diagnosis, and early achievement of cytogenetic and molecular responses are associated with better survival outcomes, whereas advanced disease phase and higher risk scores predict poorer prognosis. These findings emphasize the importance of timely initiation of therapy, continuous monitoring of treatment response, and risk-based stratification to optimize long-term outcomes in patients with CML.

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