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Clinicopathological features and risk stratification by the sokal score of patients with chronic myeloid leukemia at a tertiary care hospital in North-East India: A prospective study

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ABSTRACT

Background: Chronic myeloid leukemia (CML) is a hematologic malignancy characterized by excessive growth of myeloid cells and their progenitors. The incidence of CML is approximately 1–2/100,000 population per year. **Aims and Objectives:** The aims and objectives of the study are to determine the clinicopathological features of patients with CML and their risk stratification by the Sokal score at a tertiary care hospital in North-East India. **Materials and Methods:** This was a single-center prospective study conducted for 5 years (2018–2022). A total of 109 cases diagnosed with CML by qualitative analysis of BCR-ABL1 transcript reverse transcription-polymerase chain reaction were included in the study. The Sokal score was calculated using previously published formulae to classify the patients into different risk groups. The outcome (dead or alive) of CML patients was compared with their individual risk groups using Fisher's exact test. **Results:** Out of 109 CML patients, 73 were males and 36 were females. At the end of the study, 85 patients were alive whereas 24 died. The mean age at presentation was 42.08 ± 15.06 years. The pediatric age group comprises 1.84% of total cases. The percentages of death were higher (79.17%) in patients aged 18–59 years, followed by 20.83% in ≥60 years age group, whereas no death was recorded in the pediatric age group (<18 years). The abdominal hard lump was the most common clinical presentation, followed by abdominal fullness, weakness, and pain abdomen. The Sokal score assigns the majority (66.06%) of patients to the intermediate risk (IR) category, followed by 25.69% and 8.26% in the high-risk (HR) and low-risk (LR) categories, respectively. It was observed that the majority (28.57%) of patients died in the HR group, followed by 20.83% in the IR group and 11.11% in the LR group. **Conclusion:** The mean age of CML patients is lower than that observed in many Western countries. The Sokal score assigns the majority of patients to IR category and the maximum death were seen in the HR group.

Key words: Chronic myeloid leukemia; Clinicopathological features; Sokal score, Prospective study

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INTRODUCTION

Chronic myeloid leukemia (CML) is a hematologic malignancy characterized by excessive growth of myeloid cells and their progenitors associated with a consistent chromosome abnormality, the Philadelphia chromosome (Ph), present in over 90% of cases.[1-3] On a cytogenetic and molecular level, most CML patients demonstrate BCR-ABL1 fusion genes

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in hematopoietic progenitor cells, resulting from a reciprocal translocation between chromosomes 9 and 22; this translocation leads to a shortened chromosome 22, called the Philadelphia chromosome. Translation of the fusion products yields chimeric proteins of variable size that has increased tyrosine kinase activity and is responsible for the pathogenesis of the disease.[4]

The global yearly incidence of CML is 1–2/100,000 people and accounts for approximately 15% of newly diagnosed leukemia cases in adults with a slight male predominance.[5] CML can affect all age groups.[6-8] The median age of presentation is 45–55 years.[9] However, CML in the elderly has poor survival and advanced age is itself an independent prognostic factor. There are no biological or genetic changes that are related to aging, but age-related co-morbidity, immune defects, and bone marrow stromal changes may cause a more aggressive disease.[10] CML in pediatrics is rare and comprises 2–3% of all leukemias in childhood.[11] Young patients, regardless of prognostic factors, are generally well.[12-14] Globally, CML's incidence and death cases increased slightly in males whereas decreasing in females.[15] Imatinib, a tyrosine kinase inhibitor (TKI), inhibits the proliferation of CML lines by inhibiting BCR-ABL kinase activity and is currently being used for the treatment of CML.[16] It is predicted that imatinib will lead to a marked improvement in survival rates.[17]

Several prognostication systems have been developed to subclassify CML-chronic phase. The oldest, developed by Joseph Sokal, was derived from a cohort of patients treated with busulfan-based chemotherapy, it has been applied successfully to risk-stratify patients treated with interferon or TKIs.[18,19]

Aims and objectives

The aims and objectives of the study are to determine the clinicopathological features of patients with CML and their risk stratification by the Sokal score at a Tertiary Care Hospital in North-East India.

MATERIALS AND METHODS

This study was carried out in the Diagnostic Genetic Laboratory of the Department of Anatomy in collaboration with the Department of Pathology in a Tertiary Care Hospital in North-East India. The study was conducted after obtaining due ethical clearance from the Institutional Ethics Committee on human experimentation (No. AMC/EC/5839). This was a single-center prospective study conducted for 5 years (2018–2022). A total of 109 cases, diagnosed with CML by qualitative analysis of BCR-ABL1 transcript reverse transcription-polymerase chain reaction were included in this study. Other myeloproliferative neoplasms were excluded from the study. Sociodemographic details and clinical examination were performed and recorded for all the study participants on a predetermined pro forma after obtaining informed consent from the patient or guardians. Laboratory investigations for the blood level of hemoglobin (Hb), white blood cells (WBC), and platelet count were evaluated and investigated. The Sokal score was calculated using previously published formulae[20] to classify the patients into different risk groups using the variables: Age of the patient at presentation, spleen size (in centimeters below the left costal margin), platelet count, and the percentage of myeloblasts in the peripheral blood.

Sokal score in patients with CML is calculated by the following formula[20]

Exp (0.116 [age - 43.4])+0.0345 (spleen size - 7.51)+0.188 ([platelets/700]^2 - 0.563)+0.0887 (% blasts - 2.1).

As per the Sokal score, a patient is categorized as low risk (LR) if the Sokal score is <0.8, intermediate risk (IR) if the Sokal score is 0.8–1.2, and high risk (HR) if the Sokal score is>1.2.[20]

Statistical analysis

Data obtained were tabulated and expressed as percentages and proportions for categorical variables and mean ± standard deviation and median (range) for scale variables. Data were also presented as pie charts and bar diagrams. The outcome (dead or alive) of CML patients was compared with their individual risk groups using Fisher's exact test and $P<0.05$ was considered statistically significant. The data were analyzed by application of Microsoft Excel software version 2019.

RESULTS

Out of 109 CML patients enrolled in our study, 73 were males and 36 were females (Table 1). The mean age of the study participants was 42.08±15.06 years ranging from 15 to 80 years, with a median age at diagnosis of 42 years. The majority (82.57%) of cases were younger than 60 years whereas 17.43% were ≥60 years of age. During the study, 22.02% of patients died probably due to disease progression and at the end of the study, the remaining 77.98% of patients were alive and doing good with TKIs. The percentages of death were higher (79.17%) in patients aged 18–59 years, followed by 20.83% in ≥60 years age group, whereas no death was recorded in the pediatric age group (<18 years).

Table 1: Age and sex-wise distribution of cases, both alive and dead

Data Variables	Total number of cases (n=109)	Alive group (n=85)	Died group (n=24)
Age (years)			
Mean± standard deviation	42.08±15.06	42.24±14.20	41.54±18.10
Range	15–80	15–70	19–80
Age group (years) (%)			
Pediatric (<18)	2 (1.84)	2 (2.35)	0 (0)
18–59	88 (80.73)	69 (81.18)	19 (79.17)
≥60	19 (17.43)	14 (16.47)	5 (20.83)
Sex (%)			
Male	73 (66.97)	61 (71.76)	12 (50.00)
Female	36 (33.03)	24 (28.24)	12 (50.00)

Symptoms

The abdominal hard lump was the most common clinical presentation, followed by abdominal fullness, weakness, and pain abdomen (Figure 1). Few patients (<1%) presented with weight loss, pedal edema, chest pain, melena, or even no symptoms.

Symptoms attributable to splenomegaly included an abdominal hard lump in 42.20% of patients, abdominal fullness in 33.03% of patients, pain abdomen in 18.35% of patients, or bloating in 2.75% of patients. Splenomegaly may have contributed to the development of pedal edema or chest pain in 0.92% of patients.

Signs

The mean spleen size below the left costal margin was 7.55±2.29 cm.

Laboratory findings

Marked leukocytosis, anemia, and thrombocytosis were common features (Table 2). Anemia with a median of 7.20 g/dL Hb (3.20–12.50). The majority of the patients had Hb levels ≤7.5 g/dL. Leukocytosis with a median value of 170×10^9/L (24–460). The majority (74.31%) of CML patients had WBC counts ranging from 100–249×10^9/L.

The mean of basophils (%), blasts (%), platelets (×10^9/L), and eosinophils (%) were 4.88±2.74, 3.77±1.97, 335.45±99.14, and 3.82±1.99, respectively.

In our study, the Sokal score assigns the majority (66.06%) of patients to IR category, followed by 25.69% and 8.26% in the HR and LR categories, respectively (Table 3). It was observed that the majority (28.57%) of patients died in the high-risk group, followed by 20.83% in the IR group and 11.11% in the low-risk group (Figure 2). However, the association of risk stratification using the Sokal score with the status of the patient (dead or alive) was not found to be statistically significant (P>0.05).

Table 2: Hematological data of chronic myeloid leukemia patients

Variable	Category	No of patients	%
Hb (g/dL)	≤7.5	69	63.30
	7.6–9.4	28	25.69
	9.5–11.4	11	10.09
	≥11.5	1	0.92
Platelet count (×10^9/L)	150–449	90	82.57
	450–599	18	16.51
	600–999	1	0.92
WBC (×10^9/L)	20–99	9	8.26
	100–249	81	74.31
	250–350	13	11.93
	>350	6	5.50
Basophil (%)	<7	80	73.39
	≥7	29	26.61

Table 3: Percentage of the total sample size (n=109) categorized as low risk, intermediate risk, and high risk using Sokal score

Prognostication System	Low risk	Intermediate risk	High risk
Sokal score (%)	9 (8.26)	72 (66.06)	28 (25.69)

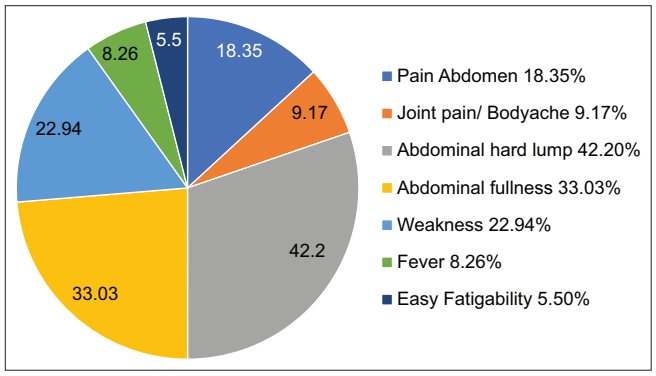

Figure 1: The main presenting clinical features of chronic myeloid leukemia patients

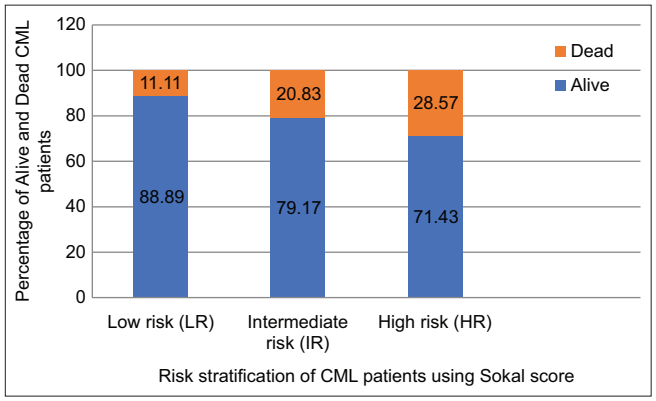

Figure 2: Comparison of the outcome (dead or alive) of chronic myeloid leukemia patients with their individual risk groups

DISCUSSION

In our study, the mean age of the study participants was 42.08±15.06 years ranging from 15 to 80 years, with a median age at diagnosis of 42 years. Most (82.57%) of the cases were younger than 60 years whereas 17.43% were ≥60 years. The findings are somewhat similar to Kantarjian et al.,[21] where 18–81 years of age range was observed among the study participants with more patients younger than 60 years of age. In many other studies, comparable mean ages were reported, such as 39.3, 40.39, 41.6, 43.3, and 43.4.[22-26] The median age at diagnosis is in accordance with Irfan and Bhurgri[27] and Mjali et al.[28]

In the present study, the majority (80.73%) of cases were adults below the age of 60 years (18–59 years). This distribution is similar to that observed by Anwer Ahmed et al.,[23] but lower than other Western studies.[8,29] The disease is observed to be uncommon in the pediatric age group in our study, with only 1.84% of patients below 18 years of age, where all are alive and doing well till date. Discordant to our findings, a study by Anwer Ahmed et al.,[23] observed 3.7% of total cases in the pediatric age group with 1.8 % and 9.4% in the alive and dead groups, respectively.

In the current study, the alive group had a mean age of 42.24±14.20 ranging from 15 to 70 years with a median age of 42 whereas in the dead group, the mean age was 41.54±18.10 ranging from 19 to 80 with a median age of 39 years, these findings are somewhat similar to that observed by Anwer Ahmed et al.[23]

The percentages of death were higher (79.17%) in patients aged 18–59 years, followed by 20.83% in ≥60 years age group, whereas no death was recorded in the pediatric age group (<18 years) in our study. However, in a study by Anwer Ahmed et al.,[23] the percentages of death were higher (75.5%) in the 18–59-year age group, followed by the patients aged ≥60 years (15.1%), whereas 9.4% of death were reported in the pediatric age group (<18 years).

CML is observed to be more common in males than in females in our study which is consistent with that reported by Kantarjian et al.,[21] Fatima et al.,[24] Irfan and Bhurgri,[27] Ganta et al.,[30] and Savage et al.,[31] but discordant with that of Anwer Ahmed et al.,[23] who observed female predominance in their study. Furthermore, in the current study, the alive group had male predominance but the dead group had an equal number of males and females, this, however, is again discordant with Anwer Ahmed et al.,[23] who found female predominance in alive patients and male predominance in the dead group.

In the present study, the mean spleen size below the left costal margin was 7.55±2.29 cm which is discordant with Aijaz et al.,[22] where the mean spleen size was 14.7±6.5 cm.

In our study, the abdominal hard lump was the most common clinical presentation whereas in studies conducted by Irfan and Bhurgri[27] pain and discomfort in the left hypochondrium was the most common presenting complaint whereas Savage et al.,[31] observed fatigue and Anwer Ahmed et al.,[23] observed fatigue and weakness as the most common presenting complaint.

In our study, majority of the patients had Hb level ≤7.5 g/dL which could be explained by the high prevalence of nutritional anemia in this part of the country, and this finding was discordant with Savage et al.,[31] who observed the majority of anemic patients with Hb ≥11.5 g/dL.

In the present study, the median value of WBC count was 170×10^9/L and the majority (74.31%) of the CML patients had their WBC count ranging from $100–249\times10^9$/L, which was comparable to the findings from the study done by Savage et al.[31]

The majority (82.57%) of CML patients had their platelet count in the range of $150–449\times10^9$/L in the current study, similar findings were reported by Savage et al.,[31] in their study. The mean platelet count of our study is in accordance with Irfan and Bhurgri.[27]

In the present study, the mean of basophils (%), blasts (%), platelets ($\times10^9$/L), and eosinophils (%) was 4.88±2.74, 3.77±1.97, 335.45±99.14, and 3.82±1.99, respectively, whereas in the study done by Aijaz et al.,[22] the mean of basophils, blasts, platelets, and eosinophils was 2.3±1.9, 6.9±8.1, 403.5±294.4, and 3.6±3.0, respectively.

Basophil <7% was seen in the majority of the CML patients in our study, a similar finding was also reported by Kantarjian et al.[21]

In our study, the Sokal score assigns the majority (66.06%) of patients to IR category, followed by 25.69% and 8.26% in the HR and LR category, respectively, which is consistent with that of Sinha et al.,[32] and Fatima et al.,[24] but discordant to that of Aijaz et al.,[22] where Sokal score assigns majority patients to HR category followed by IR and LR group and Ganta et al.,[30] where Sokal score assigns majority patients to LR category followed by IR and HR group.

Limitations of the study

As the present study was a single-center study with a relatively small number of patients, a multicentric study

over a large number of CML patients is required for a better understanding and generalization of the results.

CONCLUSION

In our study, it was revealed that patients with CML were predominantly middle-aged with a slight male preponderance. The mean age at presentation of the CML patients is lower than that observed in many Western countries, so additional epidemiological studies need to be conducted to assess for possible environmental factors accounting for earlier age at onset. The difference could, however, be due to the demographic characteristics of developing countries with lower life expectancy and a greater proportion of the young population.

The Sokal score assigns that the majority of patients to IR category and maximum death were seen in the HR group, which probably could be explained by the disease progression due to wide variation in the level of adherence with the treatment. As the present study was a single-center study with a relatively small number of patients, a multicentric study over a large number of CML patients is required to give the final verdict.

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AR- Implementation of the study protocol, data collection; UKS- Concept, design, clinical protocol, literature survey, prepared the first draft of a manuscript, editing, coordination, and manuscript revision, data analysis; SS- Review manuscript; AN- Design of study, literature survey, statistical analysis, interpretation and preparation of figures, manuscript preparation, editing, manuscript revision, and submission of article; HS- Statistical analysis and interpretation; GH- Data collection, review manuscript.

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