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COMPARISON OF PROGNOSTIC ACCURACIES OF HEMATOLOGICAL SCORING SYSTEMS FOR DETERMINING MAJOR MOLECULAR RESPONSE IN NEWLY DIAGNOSED PATIENTS OF CHRONIC MYELOID LEUKEMIA IN CHRONIC PHASE

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Abstract

Objective: *To determine frequency of Major Molecular Response in newly diagnosed patients of chronic myeloid leukemia (CML) in chronic phase undergoing treatment with Imatinib based on various scoring systems.*

Materials and Methods: *A total of 150 newly Diagnosed BCR-ABL POSITIVE CML patients in chronic phase receiving imatinib were included in this case series. The patient were recruited from the department of hematology, Holy Family Hospital Rawalpindi. The study was conducted from 11-May-2022 to 10-February-2025. Before starting treatment for CML, platelet count, blast cells percentage, eosinophils percentage and basophils percentage was determined. Clinical examination was done to assess the spleen size. Reports were assessed, and all the scores such as Sokal, Hasford, EUTOS and ELTS were calculated.*

Results: *Mean age of patients was 44.16±12.63 years. There were 90 (60%) male and 60 (40%) female patients. On comparison of prognostic accuracies of haematological scoring for MMR, 57 (82.6%) patients with low Sokal score achieved MMR, 30 (63.8%) patients with intermediate Sokal score achieved MMR and 12 (35.3%) patients with high Sokal score achieved MMR with p-value of <0.001. There were 38 (88.4%) patients with low Hasford score achieved MMR, 52 (63.4%) patients with intermediate Hasford score achieved MMR and 09 (36.0%) patients with high Hasford score achieved MMR with p-value of <0.001. There were 73 (81.1%) patients with low EUTO score achieved MMR and 26 (43.3%) patients with high EUTO score achieved MMR with p-value of <0.001. There were 56 (80.0%) patients with low ELTS score achieved MMR, 40 (64.5%) patients with intermediate ELTS score achieved MMR and*

03 (16.7%) patients with high ELTS score achieved MMR with p-value of <0.001.

Conclusion: *All scoring system such as Sokal, Hasford, AUTOS and ELTS are good in predicting the MMR in patients of CLM in chronic phase.*

INTRODUCTION

Leukemias comprise a category of serious, malignant conditions that affect the blood and bone marrow (Dong et al., 2020). Among them, chronic myeloid leukemia (CML) is classified as a myeloproliferative neoplasm and has an annual incidence rate of about two cases per 100,000 individuals (Viale, 2020). CML represents roughly 15% of all newly diagnosed cases of leukemia in adults. In the United States, it is projected that 9,280 new CML diagnoses will occur in 2024, with approximately 1,280 individuals expected to succumb to the disease, reflecting its significant impact on public health today (Jabbour and Kantarjian, 2024).

CML is a type of cancer characterized by the excessive production of blood cells resulting from mutations in a pluripotent stem cell. One of the hallmark features of this disease is the Philadelphia chromosome (Ph). This genetic marker arises from a specific translocation between chromosomes 9 and 22, noted as t(9;22)(q34;q11). This process creates the BCR-ABL1 fusion gene, which is associated with continuous activity of tyrosine kinase (Khazaal et al., 2019). The presence of this fusion gene leads to the proliferation of leukemic cells through various mechanisms that are not yet fully understood.

For individuals diagnosed with chronic-phase CML that is positive for the Philadelphia chromosome (Ph+), the latest guidelines from the European LeukemiaNet (ELN) discuss four initial prognostic scoring systems. These scoring systems assist healthcare professionals in making informed decisions about treatment approaches based on risk levels and in evaluating various outcomes in a comparative manner (Pfirrmann et al., 2020).

The Sokal and Hasford scoring systems were originally designed for individuals undergoing chemotherapy and/or interferon treatment. Their effectiveness in assessing patients treated with tyrosine kinase inhibitors (TKIs) remains a topic of debate. On the other hand, the European Treatment and Outcome Study for CML and the EUTOS long-term survival scores were created primarily for patients treated with imatinib (Zhang et al., 2022).

As treatment options for patients with CML continue to expand, there remains a significant need to enhance the accuracy of prognostic risk score metrics that inform therapeutic choices. An effective risk scoring system should be able to distinctly categorize patients into risk groups, while ensuring high sensitivity and specificity (Ganta et al., 2017). Numerous studies have thoroughly explored the clinical relevance of these prognostic systems. Some research indicates that the EUTOS score shows superior predictive capability for both progression-free survival (PFS) and overall survival (OS) when compared to the Sokal and Hasford scores (Wijaya et al., 2021).

This study aimed to evaluate the frequency of Major Molecular Response (MMR) among newly diagnosed chronic-phase CML patients receiving Imatinib treatment, utilizing various scoring systems for assessment.

METHODOLOGY:

In this descriptive case series, a total of 150 patients who met specific selection criteria were enrolled and referred to the Hematology Department at Holy Family Hospital in Rawalpindi. The study duration spanned from May 11, 2022, to May 10, 2023. The selection criteria included individuals aged between 10 and 70 years, all newly diagnosed with CML that was positive for BCR-ABL, and who were receiving treatment with imatinib. Patients in the accelerated phase or blast crisis of CML, as well as those who had previously undergone any cytotoxic treatment, were excluded from the study.

Prior to initiating treatment for CML, blood samples were collected from each patient using a 3cc BD syringe, adhering to strict aseptic techniques. These samples were then placed in vials containing EDTA for preservation. A thorough laboratory analysis was conducted to evaluate platelet counts, the percentage of blast cells, eosinophils, and basophils. Additionally,

a clinical examination was performed to determine spleen size. The results were reviewed, and scores were computed according to the established formulae of the scoring system, allowing for the stratification of patients into appropriate risk categories. We calculated the Sokal, Hasford, EUTOS, and ELTS scores and stratified the patients into different categories on the basis of scores.

Following 12 months of treatment, patients were re-evaluated in the outpatient department (OPD) to assess their prognosis using PCR to measure the BCR-ABL gene. The MMR was analyzed and compared against the predictive values of different scoring systems.

Results:

The demographic and clinical characteristics from the baseline study present several important findings. Participants in the study have an average age of 44.16±12.63 years, indicating a varied age range. The gender distribution shows that males represent a significant majority at 60% of the cohort, totaling 90 individuals, while females account for 40%, with 60 individuals included. In terms of clinical measurements, the average size of the spleen among participants is noted to be 9.24±4.23 cm. Looking at hematological parameters, the average platelet count was 457.30 × 10^9/L. Furthermore, the study reveals a mean blast percentage of 2.35% and a myeloblast percentage averaging at 32.35± 6.93%. The eosinophil percentage is on average 0.78%, while the basophil percentage is recorded at 2.25±1.33% (Table 1).

The frequency of risk stratification using various scoring systems is summarized in Table 2. The Sokal Score categorized 69 patients (46.0%) as low risk, 47 patients (31.33%) as intermediate risk, and 34 patients (22.67%) as high risk. In comparison, the Hasford Score identified 43 patients (28.67%) in the low-risk group, while the majority, 82 patients (54.67%), were classified as intermediate risk, and 25 patients (16.67%) were considered high risk. The EUTOS Score presented a different distribution, identifying 90 patients (60.0%) as low risk and 60 patients (40.0%) as high risk, with no individuals classified as intermediate risk. Finally, the ELTS Score showed that 70 patients (46.67%) fell into the low-risk category, 62 patients (41.33%) were classified as intermediate risk, and 18 patients (12.0%) were categorized as high risk (Table 2).

Out of 150 patients, 99 patients (66%) achieved a MMR while 51 patients (34%) failed to achieve a MMR (Figure 1).

On comparison of prognostic accuracies of hematological scoring for MMR, 57 (82.6%) patients with low Sokal score achieved MMR, 30 (63.8%) patients with intermediate Sokal score achieved MMR and 12 (35.3%) patients with high Sokal score achieved MMR with p-value of <0.001. There were 38 (88.4%) patients with low Hasford score achieved MMR, 52 (63.4%) patients with intermediate Hasford score achieved MMR and 09 (36.0%) patients with high Hasford score achieved MMR with p-value of <0.001. There were 73 (81.1%) patients with low EUTO score achieved MMR and 26 (43.3%) patients with high EUTO score achieved MMR with p-value of <0.001. There were 56 (80.0%) patients with low ELTS score achieved MMR, 40 (64.5%) patients with intermediate ELTS score achieved MMR and 03 (16.7%) patients with high ELTS score achieved MMR with p-value of <0.001 (Table 3).

Table 1. Baseline Study Characteristics.

Variable	Value
Age (Years)	44.16±12.63
Male Gender (%)	90 (60.0%)
Female Gender (%)	60 (40.0%)
Spleen Size (cm)	9.24±4.23
Platelet count ($\times 10^9$/L)	457.30±272.09
Blast percentage (%)	2.35±1.59
Myeloblast percentage (%)	32.35±6.93
Eosinophil percentage (%)	0.78±0.36
Basophil percentage (%)	2.25±1.33

Table 2. Frequency of Risk Stratification according to different Scoring Systems.

Sokal Score	
Low Risk	69 (46.0%)
Intermediate Risk	47 (31.33%)
High Risk	34 (22.67%)
Hasford Score	
Low Risk	43 (28.67%)
Intermediate Risk	82 (54.67%)
High Risk	25 (16.67%)
EUTOS Score	
Low Risk	90 (60.0%)
High Risk	60 (40.0%)
ELTS Score	
Low Risk	70 (46.67%)
Intermediate Risk	62 (41.33%)
High Risk	18 (12.0%)

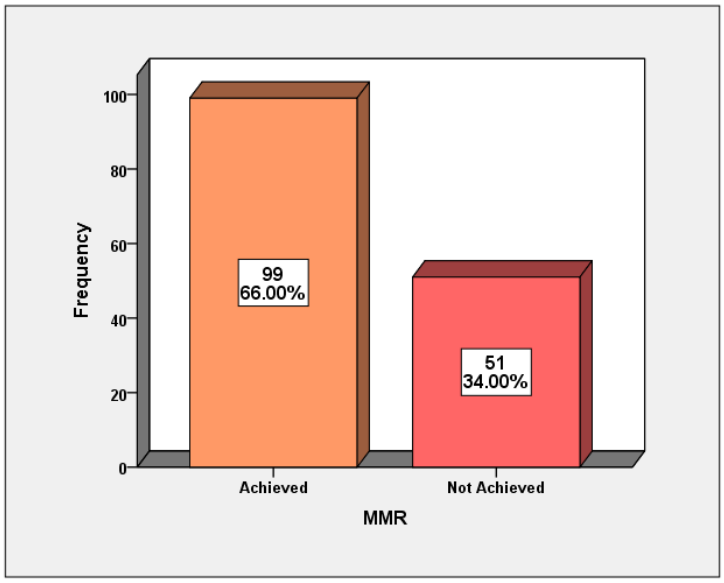

Figure 1. Frequency of Major Molecular Response (MMR).

Table 3. Comparison of Prognostic Accuracies of Hematological Scoring for Determining Major Molecular Response (MMR).

Sokal Score	MMR		P-value
	Achieved (N=99)	Not Achieved (N=51)	
Sokal Score			
Low	57 (82.6%)	12 (17.4%)	
Intermediate	30 (63.8%)	17 (36.2%)	
High	12 (35.3%)	22 (64.7%)	<0.001
Hasford Score			
Low	38 (88.4%)	05 (11.6%)	

Intermediate	52 (63.4%)	30 (36.6%)	
High	09 (36.0%)	16 (64.0%)	<0.001
AUTOS Score			
Low	73 (81.1%)	17 (18.9%)	
High	26 (43.3%)	34 (56.7%)	<0.001
ELTS Score			
Low	56 (80.0%)	14 (20.0%)	
Intermediate	40 (64.5%)	22 (35.5%)	
High	03 (16.7%)	15 (83.3%)	<0.001

DISCUSSION:

Prognostic scoring systems play a crucial role in assessing risk profiles among patients with CML, guiding treatment decisions effectively. Over the years, the methods used for prognostication have advanced significantly, leading to the creation of various scoring systems aimed at utilizing clinical experience for better management of CML. These systems were usually formulated through logistic regression, incorporating a range of clinical and hematological factors identified at diagnosis. While commonly used prognostic scores have demonstrated inconsistent correlations with achieving MMR (Dybko et al., 2016; Bonifacio et al., 2014). There has been a lack of studies that rigorously compare the validated scoring systems in terms of overall survival (OS) and event-free survival (EFS) for CML patients starting treatment with frontline imatinib. Furthermore, the comparative application of these established prognostic scores and an evaluation of their utility—particularly in light of discrepancies in risk stratification—remains largely unaddressed in existing research (Chhikara et al., 2018; Banjar and Alsobhi, 2017).

The EURO, Sokal, and EUTOS scoring systems are utilized to evaluate the severity of the disease. Historically, both the Sokal and EURO scores were seen as valuable prognostic tools before the introduction of imatinib (Specchia et al., 2021). However, the Sokal score remains highly effective in forecasting outcomes for patients receiving imatinib and later-generation tyrosine kinase inhibitors (TKIs). In 2011, the EUTOS score was introduced, as it was deemed inappropriate to rely on a scoring model created prior to the availability of imatinib (Hasford et al., 2011). The introduction of imatinib has led to its application across various age demographics in patients with CML. As a result, age—which was previously considered a significant risk factor in earlier scoring systems—has been eliminated from the EUTOS score. This new scoring approach simplifies the assessment by focusing solely on two factors: the percentage of basophils in the blood and the size of the spleen. While the influence of basophil levels and spleen dimensions on CML prognosis remains somewhat ambiguous, research suggests a correlation between the degree of basophilia and the stage of the disease. Additionally, it has been found that Ph+ cells in the spleen exhibit different behaviors compared to those in the bone marrow (Schemionek et al., 2012).

When evaluating the achievement of Major Molecular Response (MMR) at the one-year mark among low-risk EUTOS patients, various studies reported figures of 61%, 56%, and 51% (Than et al., 2012; Yahng et al., 2012). In contrast, our research documented an impressive 81.1% MMR rate. The variation between high-risk and low-risk subsets was statistically significant, aligning with the findings of Yahng et al. However, no significant differences were found within the Sokal risk group subsets (Yahng et al., 2012).

In our study, MMR was achieved in 82.6% patients having low Sokal score and in 35.3% patients having high Sokal score. Similarly, MMR was achieved in 88.4% of patients having low Hasford scores, in 63.4% of patients having intermediate scores, and in 36% of patients having high Hasford scores. Similar trends were observed for AUTOS and ELTS scores.

Numerous studies have thoroughly examined the clinical importance of various prognostic scoring systems. Some research indicates that the EUTOS score has superior predictive accuracy for progression-free survival (PFS) and overall survival (OS) when compared to the Sokal and Hasford scores (Chhikara

et al., 2018; Tao et al., 2014). Additionally, another study successfully validated the ELTS score using a separate patient cohort, demonstrating better discrimination between risk groups compared to the Sokal score. The accuracy comparisons revealed that Sokal had an accuracy of 62.10% against 48.42%, while the Hasford score showed 67.37% versus 58.94%, and the ELTS score had 62.10% compared to 61.05%. The European LeukemiaNet (ELN) has indeed proposed categorizing patients into low-risk (which includes intermediate risk) and high-risk groups for the management of CML (Banjar and Alsobhi, 2017).

Our study has several limitations that should be acknowledged. Firstly, there is an unequal distribution of cases across the Sokal risk categories, with a significant majority falling into the low-risk group. Secondly, the assessment of patient compliance relied solely on their self-reported responses, lacking any objective measurement to confirm adherence.

CONCLUSION:

All scoring system such as Sokal, Hasford, AUTOS and ELTS are good in predicting the MMR in patients of CLM in chronic phase.

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