

# Prognostic and Predictive Implications of Sokal Scoring System in Newly Diagnosed Chronic Myeloid Leukaemia Patients

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## ABSTRACT

**Objective:** To assess the predictive utility of the Sokal scoring system for determining disease prognosis in newly diagnosed patients with chronic myeloid leukemia (CML).

**Methodology:** This comparative cross-sectional study was conducted at the Armed Forces Institute of Pathology, Rawalpindi, Pakistan, from September 2021 to September 2022. The study included all newly diagnosed Philadelphia-positive chronic myeloid leukemia (CML) patients. Patients with CML in the accelerated and blast phases, as well as those with atypical CML, were excluded. Gender was considered as a qualitative variable of interest, while platelet count, spleen size, age, and percentage of myeloblasts in the peripheral blood were the quantitative variables of interest. These variables were documented using preformed data sheets, and the prognostic class of each patient was recorded. Follow-up assessments were conducted after 3 months for patients who received the same tyrosine kinase inhibitor (TKI) therapy to avoid bias.

**Results:** A total of 62 patients were included in the study, with a mean age of 46±5 years. According to the Sokal scoring system, 20 (32%) of 62 patients were classified as low-risk, 34 (54.8%) as intermediate-risk, and 8 (12.9%) as high-risk.

**Conclusion:** The routine implication of traditional prognostic scoring systems, such as the Sokal score, is beneficial for stratifying CML patients into different risk groups due to its cost-effectiveness. Regression in Sokal score grades was observed after 3 months of TKI therapy.

**Keywords:** Chronic Myeloid Leukemia (CML), Sokal scoring system, Philadelphia.

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## Introduction

Chronic Myeloid Leukemia (CML) is a proliferative clonal hematopoietic disorder of stem-cell origin. It is specified by the occurrence of chromosomal translocation t(9;22)(q34;q11) which results in the development of the Philadelphia chromosome, containing the BCR-ABL1 fusion gene.<sup>1</sup> There are three standard stages of chronic myeloid leukaemia at present: chronic, accelerated and blast phases.<sup>2</sup> Patients with CML in the chronic phase (CML-CP) have shown to have a more favorable outcome with conventional EUTOS and Hasford. On the other hand, CML patients who are in the accelerated phase (also known as CML-AP) or blast phase (also known as CML-BP) have poor outcomes with conventional therapy.<sup>3</sup> This

particular research covered Philadelphia-positive (Ph+) CML patients who were in the chronic phase of their disease. The risk stratification of CML patients can be carried out using various widely used prognostic scoring systems. Among them, the Sokal risk score is the most salient of the scoring systems. Thus, the predictive and prognostic efficacy of the Sokal score was assessed in this particular study. The origin of the Sokal score was in 1984 when there was a need to arrange patients treated with hydroxyurea into multiple risk groups.<sup>4</sup> The patient's count of platelets, age, the proportion of myeloblasts in the peripheral blood, and spleen size are required as baseline information for calculating the Sokal risk score.<sup>5</sup> According to the Sokal Scoring System, participants in this research were categorized into three

risk populations: low-risk (LR), intermediate-risk (IR), and high-risk (HR).<sup>6</sup> There are several treatment methods available for CML patients, with allogeneic stem cell transplantation (SCT) being the only curative treatment for these patients.<sup>7</sup> However, with the launch of new targeted therapy with oral tyrosine kinase inhibitors (TKI), the approach towards the use of allogeneic stem cell transplantation (SCT) as a treatment option has shifted towards TKIs. The rate of long-term survival outcomes of CML patients has improved significantly with the onset of use of tyrosine kinase inhibitors (TKI).<sup>8</sup> Imatinib, the first BCR-ABL-targeting medication, was authorized for use as the first course of therapy for CML patients with a positive Philadelphia chromosome (Ph).<sup>9</sup> In this trial, patients recently diagnosed with CML-CP were administered Imatinib mesylate, a competitive inhibitor of BCR-ABL tyrosine kinase. Significant evidence suggests that Imatinib has been shown to generate both cytogenetic and hematological remissions.<sup>10</sup>

This study employed the Sokal scoring system to arrange recently diagnosed Philadelphia-positive Chronic Myeloid Leukaemia (CML) patients into three distinct risk entities: low, intermediate, and high-risk, followed by their assessment after 03 months post-TKI therapy with Imatinib.

## Methodology

This study employed a comparative cross-sectional research design, and it was done at Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan, from September 2021 to September 2022. Data collection was done after getting approval from the Ethical Review Committee. All participants gave both verbal and written informed consent to be included in the study. A total of 62 subjects were employed in the current investigation. All the subjects were evaluated both at the time of presentation and three months after completing TKI treatment.

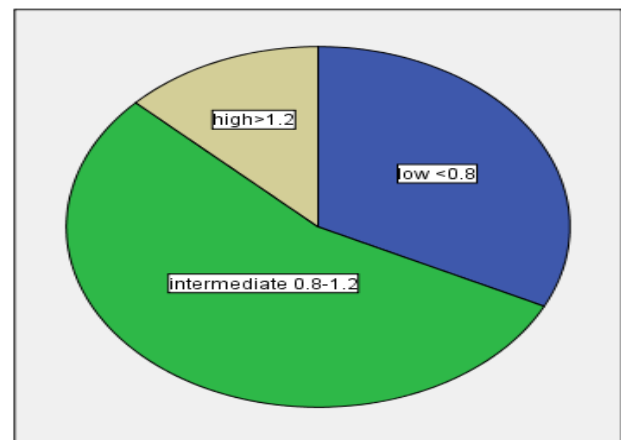
Patients recently diagnosed with Philadelphia- positive chromosome (Ph+) the chronic phase of the CML disease were included in this study. Philadelphia-negative CML patients, patients in the accelerated and blast stages as well as already diagnosed cases undergoing treatment with other TKIs were excluded from this research.

The clinical data, including the age and gender of the patient, a brief history (presenting symptoms at the time of diagnosis), general physical examination (organomegaly), baseline complete blood count, peripheral blood film findings, bone marrow examination and biochemical profile were documented on a predefined pro forma.<sup>8</sup> The

above-mentioned clinical data of every patient was documented again on a similar pro forma after three months of TKI therapy (imatinib therapy). Statistical Package for Social Sciences (SPSS) version 24.0 was used for the analysis of the data. The qualitative variables were condensed as frequency and percentages, and the quantitative variables as mean $\pm$ SD. The Sokal score of each patient was calculated based on the formula given below.

Sokal score =  $\text{Exp} [0.0116 \times (\text{age in years} - 43.4) + 0.0345 \times (\text{spleen size} - 7.51) + 0.1889 \times (\text{platelet count}/700)^2 - 0.563] + 0.0887 \times (\text{blast cell counts} - 2.10)$ , where Exp is the exponential function.<sup>9</sup> All the patients received the first line of TKI therapy -Imatinib 400mg daily, with the dose tailored per patient as deemed necessary by the treating physician.<sup>10</sup> The Sokal score risk categories were assessed -Low, Intermediate, and High (Figure 1.), at the time of diagnosis and following 03 months of TKI therapy.<sup>11</sup>

**Figure 1. Pie chart showing Sokal score risk groups.**



## Results

The total count of CML-CP patients employed in this study was 62, with a male-to-female ratio of 1.5:1. The age range at presentation ranged from 07 to 87 years, with a mean age of 46 years. The median amount of time between the patients' chronic stage diagnosis and the beginning of TKI treatment was 90 days. At diagnosis, the clinico-hematological parameters taken into account are listed in table-I.<sup>12</sup>

At the time of the diagnosis, the risk categorization by the Sokal score included: 20 out of 62 patients (32%) as a low-risk category, 34 patients (54.8%) as an intermediate-risk category, and 8 (12.9%) as a high-risk category. Table-II lists the proportion of patients falling into each risk category using the Sokal scoring system.

**Table I: Baseline characteristics/variables.**

Data Variables	Value (median)	Range
Age (years)	46	7-87
Gender (male: female)	Male predominance	1.5:1
Platelet count( $10^9/L$ )	400	140-700
Peripheral blast (%)	2	1-7
Spleen size (cm)	12	10-18
Hb (g/L)	12	7-15
Eosinophils (%)	5	0-13
Basophils (%)	6	0-15

This risk stratification process was again carried out after 03 months on the same patients to determine the predictive efficacy of the Sokal score in this particular patient group undergoing treatment with Imatinib. The results obtained were as follows: 20 out of 62 patients who were already in the low-risk category had low-risk disease after the 3-month therapy; out of 34 intermediate-risk score patients at baseline, 12 became low-risk while 22 persisted in the intermediate-risk group. Out of 8 patients stratified as high-risk at baseline, 5 became intermediate-risk, while 3 remained in the high-risk category post 3 months of treatment. (Table-III)

**Table II: Patient distribution according to risk scores in the present study.**

Risk Group	Sokal Score
Low (%)	20 (32%)
Intermediate (%)	34 (54.8%)
High (%)	8 (12.9%)

**Table III: Comparison of Sokal score at baseline and after 3 months.**

SOKAL SCORE	At start of treatment	After 3 months of treatment	p-value
Low Risk	20 (32%)	32 (52%)	<0.001
Intermediate Risk	34 (55%)	27 (43%)	<0.001
High Risk	08 (13%)	3 (5%)	<0.001

## Discussion

CML is a myeloproliferative malignancy comprising of three phases, namely the chronic (CP), accelerated (AP) and blast (BP) phases. The early chronic phase has the best prognosis, while the later advanced phases (accelerated and blast) do not show satisfactory outcomes with conventional therapy.<sup>11</sup> Numerous techniques, including cytogenetics analysis for identifying the Philadelphia chromosome and genome molecular analysis, have been developed to help determine the prognosis of newly diagnosed patients of CML-CP at the initial diagnostic stage.<sup>12</sup> However, due to the need for technical expertise and cost constraints, the use of these modalities is not seen in routine. Hence, various scoring models based on easily

accessible clinical and hematological parameters as well as a variety of statistical tests and endpoints, have been designed and are in use for the prognostic evaluation of CML-CP patients at the initial stage of their diagnosis.<sup>13</sup> TKI therapy is the most commonly used treatment modality for Chronic Myeloid Leukemia patients in the current time.<sup>14</sup> TKI therapy has greatly enhanced the prognosis of CML-CP patients, and after approximately 6-7 years, they are to improve the survival rate by around 100% in imatinib-responsive patients.<sup>15,16</sup>

260 CML patients who were in the chronic phase were investigated by Sunita *et al.* in New Delhi. The median age at diagnosis was 35 years and the male-to-female ratio of patients was 1.6:1. In this study, it was assessed that out of 260 patients, 35.38%, 48.07%, and 16.5% patients were categorized into low-, intermediate- and high-risk scores which was in concordance with the current study.<sup>17</sup> Amna *et al.*, studied 260 CML-CP Ph-positive patients at Sheikh Zayed Hospital in Lahore with a median age of  $49.18 \pm 20.33$  at the initial stage of diagnosis. The male-to-female ratio in this study was 1.2:1. This study stated that among the CML patients at baseline, 172 (66.2%) patients had low risk, while the intermediate risk was observed among 76 (29.2%) patients and high risk among 12 (4.6%) patients. While the risk categorization in the current study at the time of diagnosis was as follows; 20 (32%) in low risk, 34 (54.8%) in intermediate risk, and 8 (12.9%) in high-risk class. This showed that calculations at the time of diagnosis by Amna *et al.* were quite different from the current study. According to results from the study by Amna *et al.*, 8 out of 76 patients who were previously at intermediate-risk at baseline switched to the low-risk group, while 68 stayed in the intermediate-risk group. This means that out of 172 patients who were in the low-risk category at the initial stage, they stayed in that group following TKI treatment. After three months of therapy, 7 out of 12 patients moved from the high-risk to the intermediate-risk team, while 5 were still in the group with the highest risk. These results were coherent with the current study.<sup>18</sup>

A study by Waheed *et al.* recruited 128 patients for their research. The ratio of the male-to-female research population was 1:1. According to Sokal risk score system, these 128 patients were categorized as: 9(7%) low-risk class, 59 (46%) intermediate-risk class, and 60 (47%) high-risk class. In this study, these patients were treated with Nilotinib, while in the current study, Imatinib was used to treat the subjects. Median follow-up in this study was done after three months, just like the recent

study; 115 (90%) of the patients achieved complete hematological response (CHR), while the Major Molecular Response (MMR) was observed in 80 patients at 12 months. MMR was substantially higher (p-value 0.05) among patients in the low Sokal risk population compared to the intermediate/high Sokal risk population. Similar to the present trial, none of the patients in the lower-risk population had unsuccessful treatment. However, even after a full year of therapy, 11 and 21 patients in the moderate and high-risk populations, respectively, failed to demonstrate improved outcomes.<sup>19</sup>

Another study by Eri Yamamoto *et al.* assessed 145 CML-CP patients diagnosed between 2001-2011 and treated with Imatinib. In that particular study, the median follow-up time was 57 months. This research determined the risk scores among the CML-CP patients using three scores: EUTOS, Hasford, and Sokal scores. While in the current research, risk stratification was done using the Sokal score only. Based on the EUTOS score, 129 (89%) had low risk, and 16 (11%) had high risk. 66 and 60 individuals, 52 and 72 individuals, and 27 and 13 individuals, respectively, exhibited low, moderate, and high risks based on the Hasford and Sokal grading approaches. According to this research, the Sokal and Hasford scores were reliable indicators of prognosis; however, the EUTOS score failed to predict MMR and CCyR (complete cytogenetic response) at 12 and 18 months, as well as the PFS (progression-free survival), EFS (event-free survival), and OS (overall survival) rates. This study also stated that the multiple parameters involved in the calculation of Sokal and Hasford scoring systems were similar; however, the EUTOS score only comprised of two parameters: spleen size and basophil count. Age, blast cell count and platelet count included in the Sokal and Hasford systems but not in the EUTOS score system, might have some kind of prognostic impact on CML-CP patients.<sup>20</sup>

This demonstrated the availability of many risk stratification scores, with the Sokal score system ranking as one of the top scoring systems for the prognosis of Chronic Myeloid Leukemia. This score is helpful for risk stratification, both at the time of diagnosis and after therapy with TKIs.

## Conclusion

It is concluded that Chronic Myeloid Leukemia patients can be easily designated into risk categories using the Sokal risk score, whose predictive efficacy has been found among the CML-CP patients in the imatinib era.

Regression in the grades of the Sokal score has been observed after 03 months of treatment with the TKI therapy. As a result, it is an economical approach that should be regularly used, especially in circumstances when the cutting-edge assessment methods to evaluate the response of CML patients to TKI treatment are unavailable.

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