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Research Article

Validations of Prognostic Scoring Systems in Iraqi Patients with Chronic Myeloid Leukemia in Single Center

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ABSTRACT

Chronic myeloid leukemia and known as chronic myelogenous leukemia (CML) is one of the indolent myeloproliferative neoplasms. It is characterized by the presence of the Philadelphia chromosome, a translocation between chromosomes 9 and 22 or BCR-ABL1 gene. Consistency in prognostic scores used to estimate the risk group of CML patients before therapy commencement can increase clinician trust in the treatment decision and play important role in modern medicine for CML changing treatment modalities. Inconsistency in prognostic scores occurs where two different risk categories are applied to the same chronic myeloid leukemia (CML) patient. The aims of this study were to validate the effectiveness of Sokal, Euro, EUTOS and ELTS scoring systems in predicting the outcome in Iraqi CML-chronic phase (CML-CP) patients treated with Tyrosine kinase inhibitors (TKIs) in Karbala city in Iraq and evaluate characteristics of CML patients and their molecular response. Seventy-one patients with CML were recruited in this retrospective and prospective study from April 2017 to March 2018, the Center of Oncology for Hematology of Al-Hussein Medical City in Karbala, Iraq. They were evaluated from clinical point of view and their laboratory data, and molecular responses to TKIs based on polymerase chain reaction were analyzed. The median age of participants was 43 years; the male: female ratio was 1.03:1. In low risk category were 44, 41, 64, and 46 from 71 patients of them Sokal; Euro; EUTOS; ELTS scores respectively. In intermediate risk were 15, 22, 17 of 71 patient of them Sokal; Euro; ELTS scores respectively, and in high risk were 12, 8, 7, 8 from 71 patients of them Sokal; Euro; EUTOS; ELTS scores respectively. Follow- up of 30 patients who newly diagnosis was completed treated with TKIs in 3 & 6 months, 20 (66.7%) versus 28 (93.3%) achieved complete hematological response (CHR), while 9 (30%) versus 1(3.3%) were non CHR (xCHR), and 1 (3.3%) was (CCyR or MMR). In the current study, CML patients were at a younger age of onset, scoring systems are the most reliable clinical prognostic method evaluating CML patients indicates. That Sokal, Euro, EUTOS and ELTS scoring systems are effective in predicting early treatment response.

Keywords: Chronic myeloid leukemia; Prognosis, Sokal; Euro, EUTOS, ELTS scores.

INTRODUCTION

Chronic Myeloid Leukemia (CML) is a hematopoietic stem cell disease, characterized by a reciprocal translocation between chromosomes 9 and 22, resulting in the formation of the Philadelphia chromosome (Ph). This translocation t (9;22) results in the head -to-tail fusion of the breakpoint cluster region (*BCR*) gene on chromosome 22 at band q11 and the Abelson murine leukemia (*ABL*) gene located on chromosome 9 at band q34. The product of the fusion gene (*BCR-ABL*) is believed to play a central role in the initial development of CML[1]. This genetic abnormality was first named at 1960 so it was one of the first malignancies to be linked to a clear genetic abnormality[2]. In less than last 10 years, the prognosis of CML has changed from that of a fatal disease to a disorder amenable simply to lifelong oral medication and compatible with a normal lifespan. This change has been made possible by a deep understanding of the molecular pathogenesis and a determination to develop targeted and selective drugs[3]. CML is the most common of chronic myeloproliferative disorders. It accounts for about 15–20% of all cases of adult leukemias, but less than 5% of all childhood leukemias[4]. Family history does not play any role in causation of chronic myeloid leukemia so CML does not run in families[5]. CML can be easily diagnosed in an appropriate clinical setting with view of typical hematology and morphology findings. It could be diagnosed in the presence of splenomegaly, leukocytosis (with predominance of neutrophils and myelocytes), and hypercellular bone marrow (BM), which is mainly granulocytic or granulocytic and megakaryocytic hyperplasia[6]. Monotherapy with a TKI that targets the ABL1 kinase is currently regarded as standard treatment for CML- chronic and accelerated phase. Patients with CML- blast phase may be treated either with a TKI alone or in combination with chemotherapy[7]. TKIs including imatinib and nilotinib have greatly improved CML prognosis. In the pre TKI era, the 5-year CML overall survival (OS) with chemotherapy and interferon was 42% and 57%, respectively, with imatinib the 5-year CML OS was 89–93%[8].

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Table 1: Calculation of the relative risk of a patient with CML using clinical and hematological data obtained before any treatment

Sokal[9]	Euro [10]	EUTOS [11]	ELTS [13]
Year introduced	1984	1998	2011	2016
Predominant treatment modality	Conventional chemotherapy	IFNα-based regimens	Imatinib	TKIs era
Factors	Age Spleen size [a] Platelet count Percentage of blasts	Age Spleen size [a] Platelet count Percentage of blasts Percentage of basophils Percentage of eosinophils	Spleen size [a] Basophil count	Age Spleen size [a] Platelet count Percentage of blasts
Risk calculation	exp (0.0116× (age [years]–43.4) +(0.0345× (spleen size [cm]–7.51) + (0.188× ((platelets [109/L]/700)2– 0.563)) +(0.0887× (blasts [%]–2.10))	0.666 (when age ≥ 50 years) (0.042 x spleen size cm below costal margin) 1.0956 (when platelet count >1500 x 10^9/L) (0.0584 x blast cell % in peripheral blood) 0.20399 (when basophil % in peripheral blood ≥3%) (0.0413 x eosinophil % in peripheral blood)] X 1000.	(7× basophil [%]) +(4× spleen [cm])	0.0025 x (age in completed years/10)^3 0.0615 x spleen size cm below costal margin 0.1052 x blasts % in peripheral blood 0.4104 x (platelet count/1000)-0.5
Relative risk	Exponential of the total	Total x 1000	Total	Total
Low	< 0.8	≤780	≤ 87	≤ 1.5680
Intermediate	0.8–1.2	781–1480	N/A	1.5680–2.2185
High	>1.2	>1480	> 87	> 2.2185
Endpoint	Survival	Survival	CCyR	CML-specific survival

[a] Spleen size is measured by manual palpation and expressed as maximum distance perpendicular from costal margin.
CCyR, complete cytogenetic response; CML, chronic myeloid leukemia; ELTS, EUTOS Long-Term Survival; EUTOS, European Treatment and Outcome, Exp: Exponential Function
Study; N/A, not applicable.

Prognostic risk scores are used to predict survival at diagnosis in patients with chronic myeloid leukemia (CML) presenting in chronic phase. Until recently, risk stratification of CML patients was based on scores from the pre-imatinib era developed to predict overall survival probability. The Sokal risk score was published in 1984 and is based on outcome of patients treated with busulfan or splenectomy in combination with intensive chemotherapy[9]. The Hasford risk score, also known as the Euro score, was established in 1998 using data from CML patients receiving interferon-α therapy[10]. After the introduction of imatinib, the European Treatment and Outcomes Study (EUTOS) risk score was established in 2011 to predict the chance of achieving complete cytogenetic response (CCyR) at 18 months, as a proxy for survival[11]. The life expectancy of CML patients is currently approaching the life expectancy of the general population[12]. Since the major causes of death of CML patients are no longer CML-related, the need for baseline risk prediction has shifted from overall survival towards disease-specific mortality. In 2016, the EUTOS long-term survival (ELTS) score was introduced to predict the risk of dying of CML. It was developed using data from chronic phase CML patients diagnosed between 2002 and 2006 treated with imatinib[13].

In the current study, evaluating their main clinical presentation, the laboratory profile, we further evaluated the ELTS score as predictor for "death due to CML" in a recent population-based cohort of CML patients treated upfront with imatinib or a second generation TKI (2GTKI). The ELTS score was compared to Sokal, Euro and EUTOS scores for all three endpoints. To our knowledge, this is the first study to use data from Iraqi patients for comparing different score systems for CML

Table 2: Baseline characteristics of seventy-one participants.

Patient's characteristics	Mean ± SD		Range
Age / years	42.44± 15.91		11-70
Gender			
Male	36 (50.7%)		M/F 1.03:1
Female	35 (49.3%)		
HB (g/dL)	(11.63± 2.16)		(6.90-15.80)
WBC count (10^9/L)	(68.02± 100.75)		(3.30-440)
Eosinophils%	(3.0±3.3)		(0 -15)
Basophils %	(1.52±1.73)		(0-7)
Myeloblast%	(1.65± 4.55)		(0- 35)
PLT (10^9/L)	(298.68± 157.58)		(39-990)
Spleen size	(4.5-6.34)		(0-22.3)
Duration of Treatment (months)	Treatment n= 41	Newly diagnosis n=30	Total (n=71)
Mean ± SD	62.84±35.41	6.00±	68.84±35.41
Range	(144-12)	(6-0)	(144-0)
Type of Treatment			
Imatinib	27 (%65.9)	21(% 70)	48 (%67.6)
Nilotinib	14 (%34.1)	9 (% 30)	23 (%32.4)
Phase of disease			
Chronic phase	38 (%92.7)	30 (%100)	68 (%95.8)
Advanced phase	3 (%7.3)	0 (%0.00)	3 (%4.2)

Table 3: Patient stratification according to the 4 scoring systems.

Scores System	Relative risk	Samples		Total (n=71)	chi^2	P. Value
		Treatment (n=41)	Newly diagnosis n=30			
Sokal	Low	38 (53.5%)	6 (8.5%)	44 (62.0%)	23.27	0.000
	Intermediate	2 (2.8%)	13 (18.3%)	15 (21.1%)	8.07	**0.005**
	High	1(1.4%)	11(15.5%)	12(16.9%)	8.33	**0.004**
Total		41 (57.7%)	30 (42.3%)	71(100.0%)	38.9	**000.0**
Euro	Low	31(43.7%)	10 (14.1%)	41(57.7%)	10.76	0.001
	Intermediate	9 (12.7%)	13 (18.3%)	22 (31.0%)	0.73	0.394
	High	1 (1.4%)	7 (9.9%)	8 (11.3%)	4.5	0.034
Total		41 (57.7%)	30 (42.3%)	71(100.0%)	14.63	0.001
EUTOS	Low	41(57.7%	23 (32.4%)	64 (90.1%)	5.06	0.024
	High	0(0.0%)	7 (9.9%)	7 (9.9%)	7	0.000
Total		41(57.7%)	30 (42.3%)	71(100.0%)	10.61	0.001
ELTS	Low	35 (49.3%)	11 (15.5%)	46 (64.8%)	12.52	0.000
	Intermediate	4 (5.6%)	13 (18.3%)	17 (23.9%)	4.77	0.029
	High	2 (2.8%)	6 (8.5%)	8 (11.3%)	2	0.157
		41(57.7%)	30 (42.3%)	71(100.0%)	18.02	0.000

prognosis after the original paper by Pfirrmann et al.[13] who developed the ELTS score, However, conflict between prognostic scores is observed in some CML patients. Thus, it is important to study consistency between prognostic score categories used to allocate CML patients to risk groups in order to support clinician decision making[10].

In order to get best determination an individual's response to therapy, an initial requirement is to achieve the complete hematological response (CHR), to consider a normal peripheral blood count within 3 months of imatinib treatment. More response to treatment is subsequently monitored by series of cytogenetic assessments of the bone marrow with the aim to achieve a CCyR by 18 months. Then after evaluation of the therapeutic response is recommended by means of molecular analysis, with reverse transcriptase polymerase chain reaction (RT-PCR). Patients who get a major molecular response (MMR) equal to the reduction in BCR-ABL1 transcripts to less than 0.1% as defined on the international scale (IS), are predicted to have a significant low risk of disease bad progression as European Leukemia Net (ELN) definitions of treatment response[14].

MATERIALS AND METHODS

Patients

This was a retrospective study performed on 71 male and female CML patients (with either newly diagnosed or already treated patients) patients with CML-CP selected

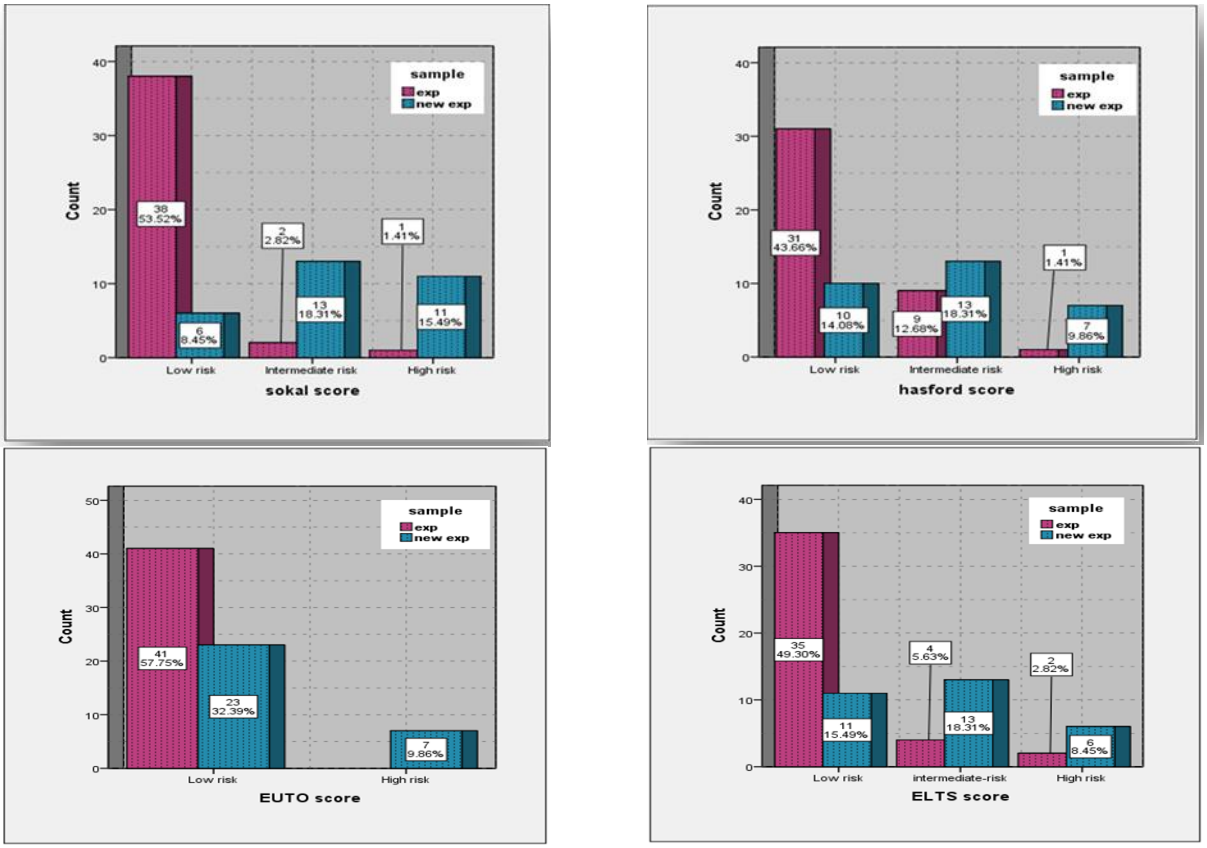

Figure 1: Baseline Sokal, Hasford, EUTOS, and ELTS scores in the study population.

consecutively who were treated with TKIs referred to the Center of Oncology for Hematology of Al-Hussein Medical City in Karbala, Iraq. The CML subjects included 30 newly diagnosed (untreated) patients (15 men and 15 women) with a mean age of 41.96 ±14.29 yr. and an age range of 19 – 65 yr. who were followed up for 3 and 6 months. Also, another 41 already diagnosed as having CML and currently receiving treatment included 21 male and 20 females with a mean age of 42.36±16.07 yr. and an age range of 11 – 70 yr. The range of duration of diseases between several months to 12 yr.

Till time of writing this article, only two types of TKIs are available in Iraq which include Imatinib (IM) and Nilotinib, Imatinib mesylate (Gleevec, Novartis) into clinical practice nearly one decade ago, has dramatically changed treatment and follow-up of CML,48 patients were started at dose of 400 mg/day. The dose was adjusted according to their tolerance and response, and 23 patients Nilotinib was administrated at 300 mg twice daily. patients were followed up every 3 months and 6 months respectively were recorded at Complete Hematological Response (CHR) and Major Cytogenetic Response (CCyR) or Major Molecular Response (MMR).

The diagnosis of CML was based on characteristic peripheral blood smear and bone marrow examination findings and was confirmed by presence of Philadelphia chromosome on bone marrow cytogenetic studies or detection of BCR/ABL translocation by polymerase chain reaction (PCR)[3]. We used the previously defined diagnostic criteria for CML-CP according to ELN 2013 recommendations[14].

Risk stratification

Sokal and Euro scores were calculated using an online link (www.leukemia-net.org/content/leukemias/cml/euro__and_sokal_score). EUTOS score was also calculated using an online link (https://www.leukemia-net.org/content/leukemias/cml/eutos_score). ELTS score was also calculated using an online link (https://www.leukemia-net.org/content/leukemias/cml/elts_score). Using the Sokal, Euro, EUTOS, and ELTS scores, we divided the patients into each risk groups. The calculation forms of each 4 scoring systems are summarized in Table 1

Follow-up-

Complete Hematologic response (CHR) was defined as platelet count <450 × 10^9/L, WBC count <10 × 10^9/L, differential without immature granulocytes, less than 5% basophils, and in addition to the disappearance of all signs and symptoms of CML including nonpalpable spleen. MCyR was characterized as combination of both complete and partial cytogenetic responses. MMR was defined as BCRABL≤ 0.1% in the quantitative RT-PCR of blood cells Treatment failure was defined as not achieving CHR after 3 months or MMR not achieved after 12 months of treatment[14,15].

Statistical analysis

All data was computed with SPSS (Statistical Package for Social Sciences) statistical software version 23. Data was presented as mean, standard deviation, median values, ranges and percentages. Chi-square test was applied to compare differences between categorical variables. P

Table 4: Predictive power of Sokal score after 3 & 6 months.

TIME	Sokal score	Response				chi^2	P. Value
		CHR	xCHR	CHR/CCyR or MMR	Total		
3 months	Low risk	4(13.3%)	1(3.3%)	1(3.3%)	6 (20.0%)	3	0.223
	Intermediate risk	11(36.7%)	2(6.7%)	0(0.0%)	13(43.3%)	6.23	0.013
	High risk	5(16.7%)	6(20.0%)	0(0.0%)	11(36.7%)	0.09	0.763
	Total	20(66.7%)	9(30.0%)	1(3.3%)	30(100.0%)	8.861	0.065
		CHR/ MCyR	xCHR	CHR/CCyR or MMR	Total		
6 months	Low risk	4(13.3%)	1(3.3%)	1(3.3%)	6(20.0%)	3	0.223
	Intermediate risk	13(43.3%)	0(0.0%)	0(0.0%)	13 (43.3%)		
	High risk	11(36.7%)	0(0.0%)	0(0.0%)	11 (36.7%)		
	Total	28(93.3%)	1(3.3%)	1(3.3%)	30(100.0%)	8.571	0.073

Table 5: Predictive power of Euro score after 3 & 6 months.

TIME	Euro score	Response				chi^2	P. Value
		CHR	xCHR	CHR/CCyR or MMR	Total		
3 months	Low risk	9(30.0%)	1(3.3%)	0(0.0%)	10(33.3%)	6.4	0.011
	Intermediate risk	8(26.7%)	4(13.3%)	1(3.3%)	13(43.3%)	5.692	0.058
	High risk	3(10.0%)	4(13.3%)	0(0.0%)	7(23.3%)	0.143	0.705
	Total	20(66.7%)	9(30.0%)	1(3.3%)	30 (100.0%)	5.826	0.213
		CHR/MCyR	xCHR	CHR/CCyR or MMR	Total		
6 months	Low risk	9(30.0%)	1(3.3%)	0(0.0%)	10(33.3%)	3	0.223
	Intermediate risk	12(43.3%)	0(0.0%)	1(3.3%)	13(43.3%)	9.308	0.002
	High risk	7(23.3%)	0(0.0%)	0(0.0%)	7(23.3%)		
	Total	28(93.3%)	1(3.3%)	1(3.3%)	30(100.0%)	8.571	0.073

value <0.05 was considered as significant.

RESULTS

This study recruited 71 patients; with a Mean ± SD (42.44± 15.91) yr., Age range was 11–70; median age was 43 years, Patient characteristics (treated and newly diagnosis) showed in Table 2 and baseline risk stratification according to Sokal, Euro, EUTOS, and ELTS scores Table 3. while male to female ratio was 1.03:1. Majority of patients presented with either a complaint of abdominal discomfort, fever or an incidental finding of leukocytosis in Complete Blood Count (CBC). patients had splenomegaly (4.5-6.34) rang (0-22.3). Mean hemoglobin level was (11.63± 2.16) g/dl, mean WBC count (68.02± 100.75) $x10^9$/L and mean platelet count (298.68± 157.58) $x10^9$/L, the mean eosinophils, basophils, and blast count was (3.0±3.3), (1.52±1.73), (1.65± 4.55) respectively. All 30 patients were in chronic phase and followed for a median duration of 6 months ,21/30 takes IM while 9/30 nilotinib. Of 41 patients had 27/41 and 14/ 41 takes imatinib and nilotinib respectively. 38/41 in chronic phase while 3/41 in advanced phase.

Table 3 and figures showed Patient stratification according to the 4 scoring systems, of 41 patients treated and 30 the newly diagnosis, by Sokal score 38/41 versus 6/30 were in low risk group, 2/41 versus13/30 were in intermediate risk, and 1/41 versus 11/30 were in high risk. By Euro, 31/41versus 10/30 low, 9/41 versus 13/30 intermediate, and 1/41 versus 7/30 high risk. By EUTOS, 41/41 versus 23/30 low, 0/41 versus 7/30 high risk, while by ELTS were 35/41 versus 11/30 low, 4/41 versus 13/30 intermediate, and 2/41 versus 6/30 high risk.

Out of 30 patients who completed 3 months of continuous treatment, 20 (66.7%) achieved complete hematological response (CHR), while 9 (30%) were non CHR (xCHR), 1 (3.3%) was complete cytogenetic response (CCyR) or Major Molecular Response (MMR) based on BCR-ABL levels. At 6 months was observed in 28 patients (93.3%) CHR, while 1(3.3%) was either xCHR, and MMR, Hematological and molecular responses are listed according to Sokal score in Table 4.

-Low risk category: 4 patients (13.3%) achieved CHR, one patient (3.3%) was either xCHR, and CCyR or MMR (p-value no significant 0.223) in 3& 6 mo.

- Intermediate risk category: 11(36.7%), and 13(43.3%) CHR in 3 &6 mo. respectively. 2 (6.7%) were xCHR in 3mo. (p-value significant 0.013).

- High risk category: 5(16.7%), and 11(36.7%) CHR in 3 &6 mo. respectively. 20 (66.7%) were xCHR in 3mo. (p-value no significant 0.763). None of the patient with intermediate and high risk Sokal score had treatment failure in 6 mo.

Predictive power of Euro after 3 & 6months (Table 5)

-Low risk category: 9 patients (30.0%) achieved CHR, one patient (3.3%) was xCHR, (p-value significant 0.011) in 3& (p-value significant 0.223) in 6 mo.

- Intermediate risk category: 8(26.7%), and 12(43.3%) CHR in (p-value significant 0.058& 0.002) 3&6 mo.

Table 6: Predictive power of EUTOS after 3 & 6 months.

TIME	EUTOS score	Response				chi^2	P. Value
		CHR	xCHR	CHR/CCyR or MMR	Total		
3 months	Low risk	18 (60.0%)	4 (13.3%)	1 (3.3%)	23 (76.7%)	21.478	0.000
	High risk	2 (6.7%)	5 (16.7%)	0 (0.0%)	7 (23.3%)	1.286	0.257
	Total	20 (66.7%)	9 (30.0%)	1 (3.3%)	30(100.0%)	7.516	0.23
		CHR/MCyR	xCHR	CHR/CCyR or MMR	Total		
6 months	Low risk	21 (70.0%)	1(3.3%)	1 (3.3%)	23 (76.7%)	34.783	0.000
	High risk	7 (23.3%)	0 (0.0%)	0 (0.0%)	7 (23.3%)		
	Total	28 (93.3%)	1(3.3%)	1(3.3%)	30 (100.0%)	0.652	0.722

respectively.4(13.3%) were xCHR, 1(3.3%) CCyR or MMR in 3 & 6mo.

-High risk category: 3(10.0%), and 7(23.3%) CHR in 3 &6 mo. respectively. 4(13.3%) were xCHR in 3mo. (p-value no significant 0.705). None of the patient with intermediate and high-risk Euro score had treatment failure in 6 mo.

Table 6 Predictive power of EUTOS after 3 & 6 months

-Low risk category: 18 patients (60.0%) achieved CHR, 4 patients (13.3%) was xCHR, one patient (3.3%) was either xCHR & CCyR or MMR (p-value significant < 0.001) in 3mo. 21(70.0%) CHR, one & (p-value significant< 0.001) in 6 mo.

-High risk category: 2(6.7%), and 7(23.3%) CHR in 3 &6 mo. respectively. 5(16.7%) were xCHR in 3mo. (p-value no significant 0.257). None of the patient with high risk Euro score had treatment failure in 6 mo.

Table 7 Predictive power of ELTS after 3 & 6months

-Low risk category: 9 patients (30.0%) achieved CHR, one patient (3.3%) was one patient (3.3%) was either xCHR & CCyR or MMR (p-value significant 0.003) in 3 & 6mo.

- Intermediate risk category: 8(26.7%), and 13(43.3%) CHR in (p-value no significant 0.405) 3&6 mo. respectively. 5(16.7%) were xCHR, in 3mo.

-High risk category: 3(10.0%), and 6(20.0%) CHR in 3 &6 mo. respectively. 3 (10.0%) were xCHR in 3mo. (p-value no significant 1). None of the patient with intermediate and high-risk ELTS score had treatment failure in 6 mo.

DISCUSSION

Patients within sample size (treated and newly diagnosis groups) were recruited in the Hematology center which is a referral center so it does not reflect the real incidence in Iraq. CML presents itself at a younger age than in western countries[16]. In the current study, the median age of patients is 42 years These results agreed with other Iraqi studies like[17] and slightly higher than that recorded by[18], who found mean age was 39.6 years.

Therapy with TKIs is needed almost for the entire life span of CML patients, and this demands the development of new scoring system and assessment of old scoring system for risk categorization and predicting the survival and response at an early stage of CML patients. Various attempts have been made to validate the superiority of the available three old scores[19-22]. Identifying the right scoring system for the prognosis of patients with CP-CML undergoing imatinib therapy is controversial. Therefore, the aim of the present study was to validate the effectiveness of Sokal, Euro, EUTOS and ELTS scoring systems in predicting the outcome in Iraqi CP-CML patients treated with TKIs.

In CML, many baseline factors have been reported to influence the response to This and survival, such as clonal chromosome abnormalities in Ph* cells and specific multidrug resistance polymorphisms[14]. However, these data were limited in other research and have not been performed in daily clinical practice. Hence, the prognostic evaluation at diagnosis is still based on the clinical features and this is the backbone of our study. In the past three decades, risk stratification for CML patients primarily relied on Sokal and Euro scores which were developed in the pre-TKI era. These two scores were also proved to be valuable in predicting prognosis in TKI-treated patients[23]. During the TKI era, EUTOS score was proposed based on more than 2000 CP-CML patients treated with imatinib-based regimens. This score was generated to stratify CP-CML patients with different cumulative probability of achieving CCyR within 18 months and different 5-year PFS[11]. Recently, EUTOS long-term survival (ELTS) score is the first long term scoring system that considered specifically CML-related death[13]. In the current study, according to the EUTOS score, 90.1% of patients were determined to have a low risk and only 9.9% were determined to have a high risk. Using the Sokal formulation, the low-, intermediate- and high-risk groups included 62, 21.1, and 16.9% of patients respectively. While using the Euro formulation, the low-, intermediate- and high-risk groups included 57.7, 31, and 11.3% of patients, respectively. The ELTS formulation, the low-, intermediate- and high-risk groups included 64.8, 23.9, 11.3% of patients, respectively. Our findings slightly higher than that recorded by[24] about three scoring, 89% of the patients were low risk by EUTOS while 11% were a high risk. Using Sokal and Euro scores, 45.5% and 41.4% of patients, 35.9% and 49.6°of patients, and 18.6% and 9% of patients were divided into. low, intermediate and high risk, respectively[24]. On the other hand, our findings are not in agreement with the study by with[25]. who found that Chinese study, according to Sokal formulation, 45.9, 35.9, and 18.2% of patients were in the low-, intermediate- and high-risk groups, respectively, while using Euro formulation, the low,- intermediate- and high-risk groups included 50, 39.1, and 10.8% of patients, respectively. While EUTOS low risk were 75% and high risk were 25%[25]. On the other hand, our findings are not in

Table 7: Predictive power of ELTS after 3 & 6months.

TIME	ELTS score	Response				chi^2	P. Value
		CHR	xCHR	CHR/CCyR or MMR	Total		
3 months	Low risk	9 (30.0%)	1 (3.3%)	1 (3.3%)	11 (36.7%)	11.636	0.003
	Intermediate risk	8 (26.7%)	5 (16.7%)	0 (0.0%)	13 (43.3%)	0.692	0.405
	High risk	3 (10.0%)	3 (10.0%)	0 (0.0%)	6 (20.0%)	0	1
	Total	20 (66.7%)	9 (30.0%)	1 (3.3%)	30 (100.0%)	5.121	0.275
		CHR/ MCyR	xCHR	CHR/CCyR or MMR	Total		
6 months	Low risk	9 (30.0%)	1 (3.3%)	1 (3.3%)	11 (36.7%)	11.636	0.003
	Intermediate risk	13 (43.3%)	0 (0.0%)	0 (0.0%)	13 (43.3%)		
	High risk	6 (20.0%)	0 (0.0%)	0 (0.0%)	6 (20.0%)		
	Total	28 (93.3%)	1 (3.3%)	1(3.3%)	30 (100.0%)	3.701	0.448

agreement with the study by either[26,27] about predictive of ELTS score[26] using ELTS formulation, the low,- intermediate- and high-risk groups included 45.5, 46.7, and 7.8%, respectively. While[27] The majority of patients 47% were categorized as low risk according to the ELTS score, 36% as intermediate risk and 17% as high risk.

During the past decade, the therapy of CML has experienced unmatched improvements of response and survival[28]. With the advent of This, CML treatment was revolutionized. Nine patients (30%) had early treatment failure no CHR with 3 months, (one patient) was no CHR response at the 6th month, (one patient) outcome after 3 &6 months of IM therapy achieve CCyR or MMR. Comparison between Sokal, Euro, EUTOS and ELTS risk groups as regard incidence of early treatment failure non CHR at 3 mo. showed that higher percentages of high Sokal score patients and lower percentages of low Euro, and ELTS score patients. In patients with early treatment failure when compared with patients with no early treatment failure CHR patients. EUTOS score risk group showed insignificant differences as regard early treatment failure incidence, these our findings are agreement with the study by with[26] CCyR has been established as the gold standard for outcome prediction within the international randomized study of interferon and IM (IRIS trial)[29] the IRIS trial reported a correlation between Sokal score and response to imatinib, with 89% and 69% of patients with a low or high risk Sokal score, respectively, obtaining CCyR[30]. in contrast to our results, we reported 3.3% of patients with a low or high risk Sokal.

The assessment of response to tyrosine kinase inhibitor (TKIs) treatment in chronic myeloid leukemia (CML) does not only reflect tumor burden at a given time but has been shown to be linked to long-term survival outcomes as well. The majority of CML patients expect an excellent survival at diagnosis[28].

However, a\ proportion of patients develop resistance and suffer from predict (CHR, CCyR, MMR) in low and high risk and failure in high risk patients. Age was an important determinant for the Sokal and Euro score. In the era of TKIs, older age appeared to be not associated with a worse outcome[31]. That might be the reason that prognostic power of Sokal and Euro scores was partly reduced.

In conclusion, still, scoring systems are the most reliable clinical prognostic method evaluating CML patients. Despite the short period of the study, TKIs showed a favorable outcome among Iraqi patients. Our study indicates that Sokal, Euro, EUTOS and ELTS scoring systems are effective in predicting early treatment response, our study evidence supporting the ELTS as an excellent risk stratification tool for contemporary CML patients treated with TKIs.

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