Original Article

Real-World Treatment Outcomes and Safety Profiles of Tyrosine Kinase Inhibitors in Iraqi Patients with Chronic Myeloid Leukemia

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ABSTRACT

Objective: To investigates the safety profile and efficacy of tyrosine kinase inhibitors in chronic myeloid leukemia patients in Al-Diwaniyah, with a particular focus on how pre-existing disease history influences adverse events and treatment outcomes.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Hematology Center, Diwaniyah Teaching Hospital, Iraq from 1st February 2025 to 30th May 2025.

Methods: Fifty-one adult patients with Philadelphia chromosome-positive chronic myeloid leukemia, receiving Imatinib, Nilotinib, or Bosutinib were assessed. Clinical response was categorized based on recent BCR-ABL1 transcript levels into complete, major, deep, loss of major, or relapse response. Safety profiles and disease history were evaluated through documented adverse drug reactions and laboratory findings.

Results: The mean age was 49.5 years with 56.9% males. Imatinib was the most used tyrosine kinase inhibitors (52.9%), followed by Nilotinib and Bosutinib (23.5% each). Imatinib showed the best efficacy with the highest complete and major molecular response rates and the lowest relapse incidence (29.4%). Nilotinib had similar efficacy and side effects, while Bosutinib showed lower responses and higher hematological toxicity. Most 41 patients reported no adverse effects; 9 experienced toxicities like diarrhea, abdominal pain, joint pain, and hair loss. While 31 had no prior medical history, others had conditions such as diabetes, hypertension, or hypothyroidism.

Conclusion: The significant differences in tyrosine kinase inhibitors response and safety among Iraqi chronic myeloid leukemia patients, emphasizing the importance of personalized treatment strategies. The findings underscore the need to consider individual patient disease history when selecting tyrosine kinase inhibitors to optimize outcomes and effectively manage adverse events.

Key Words: Chronic myeloid leukemia, Tyrosine kinase inhibitors, Safety profile, Efficacy, Adverse events, Treatment outcomes

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INTRODUCTION

Chronic myeloid leukemia (CML) stands as a paradigm of successful targeted therapy in oncology, primarily due to the transformative impact of tyrosine kinase inhibitors (TKIs).

This myeloproliferative neoplasm, characterized by the pathognomonic Philadelphia chromosome and the resultant BCR-ABL1 fusion gene, once carried a grim prognosis, with median survival in the chronic phase rarely exceeding 3-5 years. The advent of TKIs fundamentally altered this landscape, converting CML into a manageable chronic condition for a significant proportion of patients.[1]

Imatinibmesylate, the pioneering first-generation TKI, revolutionized CML management by demonstrating unprecedented efficacy in inducing hematologic and cytogenetic responses.[2] Its success paved the way for the development of second-generation TKIs, including Nilotinib, Dasatinib, and Bosutinib, designed to offer increased potency and overcome resistance or intolerance to imatinib.[3] These advancements have led to remarkable improvements in patient outcomes globally, with 5-year overall survival rates exceeding 90% in many studys.[4] Despite the remarkable success of TKIs, their long-term use is associated with various adverse events (AEs) that can significantly impact patient quality of life and adherence to treatment.[5] The

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safety profiles of different TKIs vary, and understanding these differences in real-world settings is crucial for optimizing patient management. Furthermore, patient-specific factors, including pre-existing medical conditions and disease history, can influence both the efficacy and safety of TKI therap.[6]

This study addresses a crucial aspect of CML management in Iraq by meticulously evaluating the real-world clinical efficacy and safety profiles of various TKIs (Imatinib, Nilotinib, and Bosutinib) of Iraqi CML patients from Diwaniya. Unlike some prior investigations that focused on molecular resistance mechanisms, this research specifically aims to provide a broader understanding of real-world treatment effectiveness, patient response rates, and associated adverse events. By leveraging detailed patient data, this paper seeks to contribute valuable localized insights into the practical application and outcomes of TKI therapy in a specific regional setting, thereby informing clinical practice and future research directions in CML management within Iraq and similar healthcare environments.

METHODS

The study was conducted at Diwaniya Teaching Hospital in Diwaniya, Iraq from 1st February 2025 to 30th May 2025 and consisted of 51 individuals diagnosed with Philadelphia chromosome-positive CML, aged 12 years or older, who were actively receiving at least one form of TKI therapy. Patients with documented TKI contraindications, pregnancy, or breastfeeding were excluded from the original data collection. Data collection included Demographic and disease, treatment, and Laboratory information, with clinical outcome documentation for each enrolled patient being meticulously collected. The data was entered and analyzed through SPSS-26.

RESULTS

The distribution of current Tyrosine Kinase Inhibitors (TKIs) being administered to these patients was as follows: Imatinib was the most frequently used TKI 27 patients (52.9%), followed by Bosutinib 12 patients (23.5%) and Nilotinib 12 patients (23.5%) [Table 1].

Table No.1: Demographic and clinical characteristics of patients (n=51)

Characteristic	No.	%
Age (years)	49.5±16.3	
Gender		
Male	29	57.0
Female	22	43.
Disease phase at diagnosis – chronic	49	96.0
Disease phase at diagnosis – blast	2	4.0
Imatinib treating patients	27	53.0
Nilotinib treating patients	12	23.5
Bosutinib treating patients	12	23.5

Table No.2: Distribution of response by tyrosine kinase inhibitors (TKIs)

TKIs	Loss major response	Deep response	Complete response	Major response	Relapse
Bosutinib	2 (16.7%)	1 (8.3%)	1 (8.3%)	-	8 (66.7%)
Imatinib	3 (11.1%)	6 (22.2%)	9 (33.3%)	7 (25.9%)	2 (7.4%)
Nilotinib	1 (8.3%)	1 (8.3%)	1 (8.3%)	4 (33.3%)	5 (41.7%)

Table No. 3: Toxicity profile counts and distribution by current tyrosine kinase inhibitors (TKIs)

	Imatinib	Nilotinib	Bosutinib
No adverse effect reported	24	9	8
Diarrhoea	-	1	-
Eye bleeding	-	1	-
Cramps	-	1	-
Osteopenia	-	1	-
Hair loss	1	1	1
Skin problem	-	1	-
Abdominal pain	-	-	1
Joint pain	2	1	1
Fever for 1 week	1	-	-
Git upset	-	-	1
Eye inflammation	1	-	-
Lung inflammation	-	1	-
Nasal congestion	-	1	-

Table No.4: Distribution of disease history type by current tyrosine kinase inhibitors (TKIs)

Disease History Type	No.	%
No disease history	31	62
DM+HT	6	12
Diabetic millets	1	2
Hypertension	3	6
Benign prostate hyperplasia	2	4
Hypothyroidism	1	2
Hemorrhoid	1	2
Asthma	1	2
Bechet disease	1	2
Osteoporosis	1	2
Cerebral edma	1	2
Valve replacement	1	2

The distribution of responses (complete response, major response, deep response, loss of major response, and relapse) for each TKI is summarized in Table 2. A Chi-square test of independence confirmed statistically significant association between the type of current TKI and the patient's response ($Chi^2 = 19.94$, p-value = 0.0106). Imatinib demonstrated a notably higher proportion of favourable responses, with the majority of patients achieving either a major or complete response. In contrast, Bosutinib was associated with a higher incidence of relapse. Nilotinib showed an intermediate profile, with a good proportion of major responses but also some instances of relapse. The overall toxicity profile of the patient indicated that a significant portion of patients had no recorded adverse events. Among those with reported toxicities, a range of side effects was observed. Nilotinib was associated with a broader spectrum of adverse events, including gastrointestinal issues (diarrhea), joint pain, eye inflammation, and hair loss. Bosutinib was linked to abdominal pain, while Imatinib was associated with hypertension (HT) (Table 3)

Analysis of patient disease history revealed comorbidities in a significant portion of the patients, highlighting the importance of assessing baseline health.6 of the patients presented with both HT and DM (Table 4, Figs. 1-2).

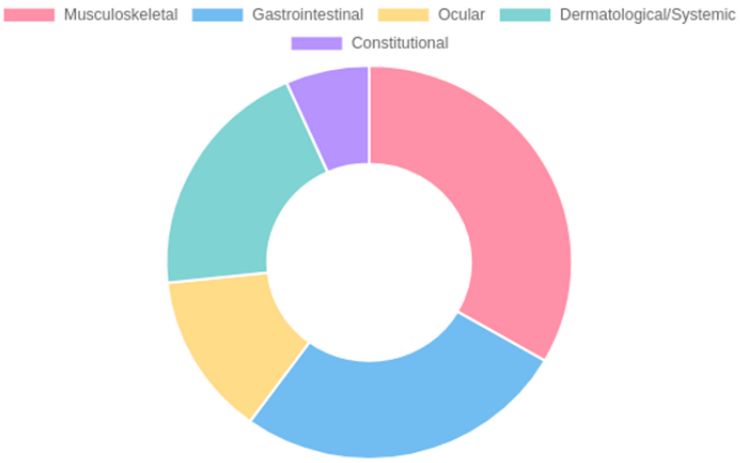

Figure No. 1: Frequency of reported adverse event types

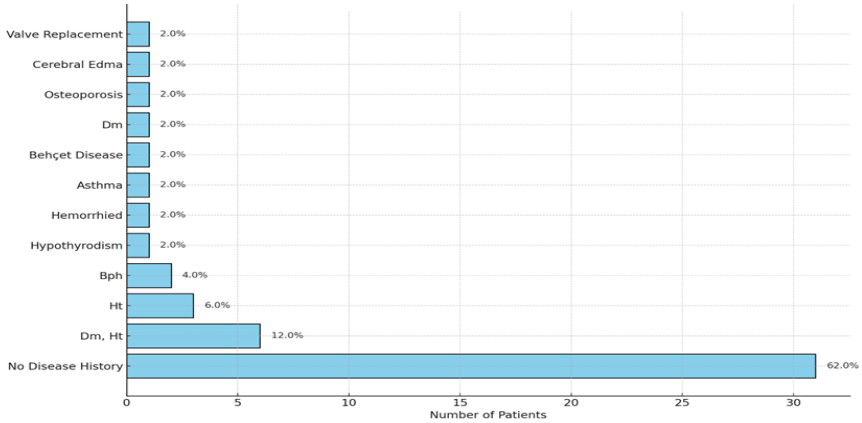

Figure No. 2: Prevalence of comorbidities among CML patients recruited. Most patients had no comorbidities, while diabetes mellitus (DM) and hypertension (HT) were the most common among those with comorbid conditions

DISCUSSION

Our findings demonstrate a clear differential in treatment outcomes among the various TKIs, particularly highlighting the superior performance of Imatinib in achieving favourable responses and maintaining remission, as evidenced by its high rates of complete and major responses and significantly lower relapse rates. Conversely, Bosutinib was associated with a higher incidence of poor responses and relapse, suggesting that its efficacy in this specific patient population, or as a treatment in the context of this study's prior therapies, may be limited.

The observed efficacy of Imatinib aligns with its established role as the first-line standard of care for CML globally.[7] Its consistent performance in this Iraqi study, despite potential differences in patient characteristics or healthcare infrastructure compared to Western populations, underscores its robust therapeutic benefits. The lower relapse rate associated with Imatinib is particularly encouraging, as sustained remission is a primary goal in CML management. This finding reinforces the importance of optimizing initial TKI selection to maximize long-term treatment success and minimize the burden of disease progression.

The less favourable outcomes observed with Bosutinib in this study warrant further investigation. While Bosutinib is a potent second-generation TKI often used in cases of resistance or intolerance to other TKIs[8], its association with higher relapse rates and poor responses in this study suggests that its application might need careful consideration and requires a kinase domain mutations screen that resistance to bosutinib. Factors such as patient selection, prior treatment history, and the specific clinical scenarios in which Bosutinib was administered could influence these outcomes. It is plausible that patients receiving Bosutinib in this study may have had BCR-ABL kinase domain mutations that are resistant to Bosutinib.

The analysis of toxicity profiles indicates that different TKIs are associated with distinct adverse event patterns. Nilotinib, for instance, appeared to be linked to a broader range of reported toxicities, including gastrointestinal and musculoskeletal issues. This is consistent with known side effect profiles of Nilotinib, which can include fluid retention, rash, and gastrointestinal disturbances.[9] Imatinib's association with hypertension is also a recognized side effect[10], though generally manageable. The impact of pre-existing disease history on TKI outcomes reveals that the high proportion of patients with no reported prior medical history (62%) might reflect a relatively healthy baseline population or limitations in historical data collection. However, the presence of common co-morbidities such as diabetes mellitus and hypertension in a significant subset of patients is clinically relevant. These conditions can influence TKI selection and management. For example, Nilotinib has been associated with an increased risk of cardiovascular events, making it a less favourable option for patients with pre-existing cardiovascular disease or risk factors.[11] Similarly, patients with pre-existing liver conditions might be more susceptible to TKI-induced hepatotoxicity.

Future research should prioritize comprehensive and standardized reporting of adverse events to better characterize the safety landscape of TKIs in this region. This study contributes to bridging the information gap regarding CML treatment outcomes inal -Al-Diwaniya, Iraq. The findings emphasize the importance of localized data to inform clinical decision-making and resource allocation. While the study's cross-sectional nature and limited sample size for certain analyses are acknowledged limitations, the results underscore the need for continued research, potentially through prospective studies with larger study and more detailed clinical and molecular data, to further refine treatment guidelines and improve patient outcomes in Iraq.

CONCLUSION

Imatinib was associated with superior response rates and lower relapse incidence, reinforcing its role as a highly effective treatment option. Conversely, Bosutinib was linked to less favourable responses and higher relapse rates within this study. While the overall toxicity data was limited, distinct patterns of adverse events were observed across different TKIs. These findings highlight the critical need for tailored treatment strategies based on local patient characteristics and available resources. The study contributes to the growing body of real- world evidence for CML management in underrepresented regions and emphasizes the importance of continued research to optimize therapeutic approaches and improve patient prognosis in Iraq.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Mohammed Jafar Al-Kabi, Doaa Husam Abdulqader
Drafting or Revising Critically:	Mohammed Jafar Al-Kabi, Bassim I. Mohammad
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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