

Therapeutic Adherence in Chronic Myeloid Leukemia in Togo

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Abstract

Once nearly fatal, chronic myeloid leukemia (CML) has become a well-managed chronic disease for most patients thanks to tyrosine kinase inhibitors (TKIs). The improvement in treatment response with TKIs has introduced a new challenge in managing CML, as with most chronic diseases: therapeutic adherence. This study was conducted to evaluate the determinants of therapeutic adherence among patients. It was a descriptive and analytical cross-sectional study conducted from March 1, 2024, to June 1, 2024, in the hematology department of the CHU Campus. Data were collected using a questionnaire. Treatment adherence was assessed using the 8-item Morisky Medication Adherence Scale. The study included 63 patients. The mean age was 45.15 ± 15.95 years (range: 9 - 81 years), and the sex ratio was 1.73. Nineteen patients (30.17%) were highly adherent, 29 (46.03%) were moderately adherent, and 15 (23.80%) were poorly adherent. Factors increasing the likelihood of high adherence included older age, family support, and satisfaction with the information provided by the physician about CML. Patients who experienced side effects were more likely to be non-adherent compared to those who did not have side effects. Proximity to the hospital, educational and socioeconomic status, medication formulation, and dosage were not significantly associated with low adherence. Ultimately, our study revealed low therapeutic adherence among our patients, and this suggests two main areas for improvement to enhance treatment adherence: a focus on therapeutic education with clear and understandable information, and optimal management of side effects.

Keywords

CML, Adherence, TKI, Lomé-Togo

1. Introduction

Chronic Myeloid Leukemia (CML) is a myeloproliferative syndrome predominantly affecting the granulocytic lineages and characterized by the presence of a clonal acquired cytogenetic abnormality, the Philadelphia chromosome (Ph1), resulting from a t(9;22) translocation. This leads to the formation of the Bcr-Abl fusion oncogenic protein, which exhibits strong tyrosine kinase activity and is responsible for leukemic transformation [1]. For a long time, CML posed a significant challenge in terms of management. However, today, thanks to tyrosine kinase inhibitors (TKIs), its prognosis has improved considerably, with the possibility of discontinuing treatment in cases of sustained deep molecular response (DMR) to achieve treatment-free remission (TFR) and potentially a cure [2]. As with all chronic conditions, the challenge of therapeutic adherence now arises, as it is a critical factor in achieving molecular remission [3] [4]. More than two decades after the introduction of TKIs into the therapeutic arsenal for CML patients in Togo and following a previous study revealing poor molecular response among patients [5], we deemed it necessary to conduct the present study to evaluate therapeutic adherence among our patients and the factors influencing it.

2. Methods

This was a descriptive and analytical cross-sectional study conducted in the hematology department of the CHU Campus over a three-month period, from March 1, 2024, to June 1, 2024. Ethical committee approval was obtained, and patient anonymity was preserved. The study included patients diagnosed with CML and receiving TKIs who provided informed consent. Data collection was carried out during semi-structured interviews using pre-established survey forms. Sociodemographic parameters, as well as those related to the therapeutic and evolutionary aspects of the disease, were documented. The 8-item Morisky Medication Adherence Scale (MMAS-8) was used to assess adherence. In cases of suboptimal adherence, the reasons for non-adherence reported by the patients were specifically recorded. Data were entered into Excel 2019 and analyzed using SPSS version 25.0 and Stata v16. For multivariate analyses, a p-value < 0.05 was considered statistically significant.

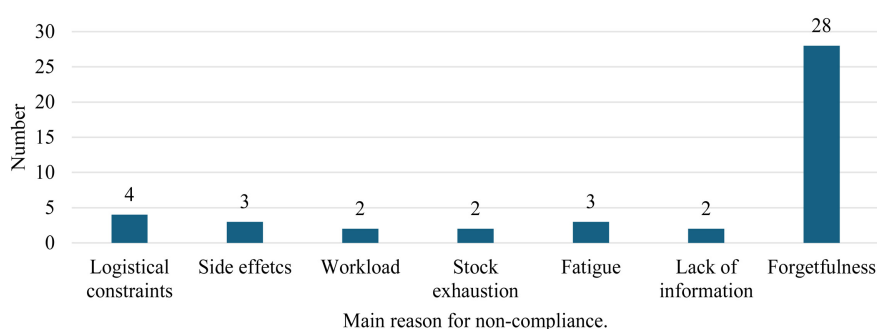
3. Results

Among the 80 patients actively followed for CML in the department, we were able to interview 63, resulting in a participation rate of 78.8%. The mean age of the patients was 45.15 ± 15.95 years, with extremes ranging from 9 to 81 years. The most represented age group was 40 to 60 years, accounting for 41.37% of participants. Regarding the disease phase, 95.23% of participants were in the chronic phase, 3.17% were in the acceleration phase, and one patient (1.60%) was in the blast crisis. In terms of treatment, 73.02% of patients were on imatinib, 23.81% on Dasatinib, and 3.17% on Bosutinib. The distribution of patients according to therapeutic adherence is presented in **Table 1**.

Table 1. Distribution of patients based on therapeutic adherence.

	Number (n)	Percentage (%)
Low	15	23.80
Medium	29	46.03
High	19	30.17
Total	63	100

The reasons for non-adherence were investigated among patients with suboptimal adherence, totaling 44 patients. Forgetfulness was the primary reason for non-adherence, accounting for 63.64% (**Figure 1**).

**Figure 1.** Reasons for non-adherence.

Statistically, older patients, those who were satisfied with therapeutic education, and those who did not experience treatment-related side effects were more adherent. Treatment duration, gender, socioeconomic status, and the specific drug had no statistical impact on therapeutic adherence.

The various factors associated with therapeutic adherence are summarized in **Table 2**.

4. Discussion

Our study is the first conducted to gain insights into adherence and the determinants of poor adherence among patients with CML. Unlike other studies carried out in sub-Saharan Africa, this study did not solely evaluate therapeutic adherence in patients on imatinib. This approach provided a comprehensive overview of therapeutic adherence in CML [6] [7]. Indeed, for more than 20 years, the free provision of TKIs through The Max Foundation's Glivec International Patient Assistant Program (GIPAP), has significantly reduced the economic burden of treatment, thereby markedly improving accessibility. This study has therefore enabled us to identify other factors that may influence patients' adherence to treatment and to take the necessary measures to improve their compliance.

The main limitation of the study was the method of questionnaire administration. Its semi-structured nature and administration by an interviewer may have

Table 2. Factors associated with therapeutic adherence.

	Therapeutic adherence (Morisky scale)				p-value
	n = 63	Low n (%)	Medium n (%)	High n (%)	
Median age (range)		32 (9 - 62)	48 (14 - 77)	49 (10 - 81)	0.04
Sex					
Male	40	8 (20)	19 (47.50)	13 (32.50)	0.63
Female	23	7 (30.43)	10 (43.48)	6 (26.09)	
Socioeconomic level					0.13
Low	42	12 (28.57)	21 (50.00)	9 (21.43)	
Middle	20	3 (15.00)	8 (40.00)	9 (45.00)	
High	1	0 (0.00)	0 (0.00)	1 (100.00)	
Satisfaction with therapeutic education					0.04
Yes	54	10 (18.52)	25 (46.30)	19 (35.19)	
No	9	7 (77.78)	2 (22.22)	0 (0.00)	
CML phase					0.02
Chronic	60	12 (20)	29 (48.33)	19 (31.67)	
Acceleration	2	2 (100.00)	0 (0.00)	0 (0.00)	
Blast crisis	1	1 (100.00)	0 (0.00)	0 (0.00)	
Molecule					0.91
Imatinib	46	10 (21.74)	21 (45.65)	15 (32.61)	
Dasatinib	15	4 (26.67)	7 (46.66)	4 (26.67)	
Bosutinib	2	1 (50.00)	1 (50.00)	0 (0.00)	
Duration of treatment					0.27
<5 years	36	10 (27.28)	13 (36.11)	13 (36.11)	
≥5 years	28	10 (35.71)	11 (39.29)	7 (25.00)	
Side effects					0.01
Yes	49	9 (18.37)	27 (55.10)	13 (26.53)	
No		6 (42.86)	2 (14.28)	6 (42.86)	

introduced biases. The questionnaire evaluates adherence subjectively: some individuals may have altered their responses out of shame or fear of judgment, or due to forgetting certain details (which is especially true for older patients). However, this method was the most appropriate, given that most of our patients did not have the educational level required to understand and complete the questionnaire independently.

Overall, our study revealed that patients with CML under follow-up in our department are generally non-adherent. These results are like those obtained in

other studies, regardless of whether the assessment tool was the same or different [6] [8]-[10].

Therapeutic adherence is a crucial element in the management of chronic diseases such as CML. Average about 50% of patients suffering from chronic diseases in developed countries adhere to their treatment regimens and this proportion is greater in developing countries [11]. A study conducted by Fentie *et al.* in Ethiopia revealed that the side effects of imatinib were the main cause of non-adherence (68.8%), while forgetfulness (13.2%) and lack of information about the medication (5.6%) were less frequently cited. This finding contrasts with the results of our study, where forgetfulness was the primary reason for non-adherence (63.6%), unlike treatment side effects (6.9%). This difference could be explained by the duration of treatment, as most patients in our study had been undergoing treatment for a longer period compared to those in Fentie *et al.*'s study [12].

Statistical analyses in our study demonstrated that advanced age, satisfaction with the information provided by the treating physician regarding CML, and the absence of side effects were significantly correlated with improved therapeutic adherence.

The impact of age on therapeutic adherence is well-documented. Some studies indicate that extreme age groups—the youngest and the oldest—are at higher risk of non-adherence. This may be attributed to various factors, such as cognitive difficulties, challenges in understanding medical instructions, or lifestyle-related barriers. In the study by Okouango *et al.*, non-adherence measured by the Medication Possession Ratio (MPR) was associated with adolescent age ($p = 0.002$) [6], whereas Kim *et al.* reported that among different age groups, older patients (≥ 70 years) had the lowest MPR ($p < 0.001$) [10]. In our study, median age increased with adherence levels. However, it would be imprudent to establish strict age thresholds for predicting adherence, likely because the most represented age group in our study was between 40 and 60 years.

It was observed that patients who were dissatisfied with the information provided by their physician tended to be non-adherent to their treatment. This finding is consistent with the results of Efficace *et al.* [8] and Geissler *et al.* [9]. These outcomes underscore the critical importance of effective communication between physician and patient to ensure optimal treatment adherence, which can directly impact treatment efficacy and, consequently, disease outcomes. Therapeutic education should therefore be an integral component of medical care, emphasizing clarity and comprehension of the information conveyed to enable patients to make informed decisions about their health.

A statistically significant correlation was identified between the occurrence of side effects and treatment adherence ($p = 0.01$). Indeed, patients experiencing adverse effects were found to be more likely to exhibit poor therapeutic adherence [13]. These findings are supported by a study conducted in Ethiopia by Fentie *et al.*, which demonstrated that patients without imatinib-related side effects were six times more likely (OR = 6.12, 95% CI: 2.31 - 14.3) to adhere to their treatment compared to those experiencing adverse effects [12]. Geissler *et al.* also

highlighted the negative impact of drug-related adverse events on therapeutic adherence, revealing that patients without side effects were more adherent (39.3% high adherence, 15.6% low adherence) than those with side effects (32.2% high adherence, 21.1% low adherence) [9].

These results suggest that measures to improve therapeutic adherence among our patients in Togo should focus on effective therapeutic education and the optimal management of treatment-related side effects. Therapeutic education should begin at the time of diagnosis and continue throughout follow-up to reinforce the importance of optimal adherence. It can also involve the patients' families. Establishing support groups for patients with chronic conditions can help provide peer support and improve adherence [14]. Regarding forgetfulness, the development of a mobile application could have a good impact, as demonstrated by Jimenez-Chala *et al.* [15].

Socioeconomic level or type of molecule had been not significantly associated with therapeutic adherence. The free provision of treatment has indeed removed the economic barrier to healthcare accessibility. Our study revealed that regardless of the molecule used, the issue of therapeutic adherence remains a challenge.

Finally, as observed in other studies [3] [10] [16] [17], the link between therapeutic adherence and outcomes was demonstrated in ours; poor therapeutic adherence is statistically associated with advanced stages of the disease. This may partly explain the low molecular response rate observed in the previous study by Padaro *et al.* [5]

5. Conclusion

In this study, we aimed to explore therapeutic adherence among patients with chronic myeloid leukemia (CML), a crucial factor for treatment success. The results showed that only one-third of these patients demonstrated good therapeutic adherence. Several influential factors were identified: advanced age, and satisfaction with the information provided by physicians emerged as key elements promoting better adherence. Conversely, treatment side effects were a major barrier, reducing the likelihood of good adherence. These findings highlight the importance of social and relational dimensions in treatment adherence and underscore the need to integrate these aspects into patient management. This study emphasizes the importance of developing personalized strategies to improve therapeutic adherence in patients with CML. An integrated approach addressing side effects and improving communication between patients and healthcare professionals could not only enhance adherence but also improve therapeutic outcomes and patient quality of life. Moving forward, it would be pertinent to design and evaluate targeted intervention programs tailored to the specific needs of these patients and to measure their long-term impact on adherence and health outcomes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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