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Living with chronic myelogenous leukemia in rural communities: Exploring factors related to tyrosine kinase inhibitors adherence with a mixed methods approach

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Abstract

Purpose: Tyrosine kinase inhibitors (TKIs) improve chronic myeloid leukemia (CML) outcomes dramatically. However, limited research exists on patient-specific, medical, and psychosocial factors influencing TKI adherence. The purpose of the study was to better understand TKI adherence among rural CML patients, using a convergent parallel mixed-method design guided by the Information Motivation and Behavioral Skills Model.

Methods: Survivors with CML participated in semistructured interviews and completed self-reported questionnaires, including demographics, perceived stress, side effects, emotional support, and self-efficacy for managing chronic conditions. Qualitative and quantitative data were collected concurrently, analyzed separately, and then integrated.

Results: Sixteen participants aged 26 to 76 years completed the study. The duration of TKI therapy ranged from 0 to 12 years (mean ± standard deviation, 5.56 ± 4.08). While all reported adherence to TKI therapy, 31% held misconceptions about treatment duration, and 38% misunderstood reasons for blood tests prior to treatment or TKI refilled. Qualitative data yielded five major themes with descriptions of the shock of diagnosis, educational experiences regarding CML and its treatment, challenges in managing side effects and refills, the importance of social support, and strategies for maintaining remission and motivating adherence to TKI.

Conclusions: This study describes the knowledge, motivations, challenges, and skills related to TKI adherence among rural patients with CML. A patient-centered approach is recommended for health care providers to improve adherence and enhance outcomes for CML patients on TKI therapy.

KEYWORDS
cancer survivors, protein kinase inhibitors, rural health, treatment adherence and compliance

The landscape of cancer treatment has shifted from traditional intravenous chemotherapy to targeted therapies, which focus on controlling the growth and proliferation of cancer cells.[1] Among these targeted treatments, tyrosine kinase inhibitors (TKIs) have revolutionized the management of various malignancies, particularly hematologic cancers. Unlike conventional chemotherapy, many TKIs are administered orally, placing the responsibility for adherence directly on the patient with minimal health care provider interactions. This shift in treatment modality presents significant challenges, particularly for rural patients who already experience greater difficulty accessing health care services. Consequently, nonadherence to TKIs has emerged as a critical issue in oncology, undermining treatment efficacy and leading to adverse clinical outcomes.[2]

A United States surveillance summary revealed that rural areas exhibit lower rates of new cancer cases compared to urban areas, yet they exhibit higher cancer mortality rates.[3] Moreover, the rural-urban disparity in cancer mortality continues to widen.[3] A systematic review of observational studies reinforces this trend, emphasizing the geographic location on cancer survival in high-income countries.[4] While adherence to TKIs has primarily been studied in relation to mortality and/or survival,[5] research on patient specific, medical, and psychosocial factors that may contribute to adherence is absent, particularly for rural patients. Poor adherence to TKIs can result in subtherapeutic drug levels, allowing tumor cells to develop resistance.[6, 7] This not only reduces the effectiveness of TKIs but also limits future treatment options, ultimately increasing the risk of disease progression and mortality. To improve outcomes, a deeper understanding of the challenges rural patients face with TKI adherence is essential. Their unique experiences must inform targeted interventions to optimize hematologic cancer treatment.

Chronic myelogenous leukemia (CML) is a hematologic disorder characterized by increased production of myeloid cells in the bone marrow,[8] that exemplifies how TKI therapy has transformed hematologic cancer treatment. Untreated CML progresses from a benign chronic phase to a fatal blast crisis within 3–5 years.[9] However, TKIs have dramatically improved prognosis, with approximately 90% of CML patients achieving complete remission and a normal lifespan.[8, 10] Despite these advances, nearly one of three CML patients do not adhere to their prescribed regimen,[11, 12] increasing the risk of drug resistance, reduced cytogenetic response, and lower survival rate.[5–7, 12, 13]

To optimize CML survivorship among rural patients, preliminary research is necessary to explore their experiences with diagnosis and treatment. The purpose of this study was to understand the current situation of TKI adherence and its influencing factors in rural patients with CML, guided by the Information Motivation and Behavioral Skills Model (IMBS).[14–16] The IMBS contains three main concepts: information, motivation, and behavioral skills. Information refers to accurate and relevant information about patients' conditions and importance of adhering to their medication regimen. In the context of CML, it includes the role of TKIs in treatment, potential side effects, and the consequences of nonadherence. Motivations encompass the emotional and attitudinal aspects of adherence, including patient beliefs, attitudes, support, perceived benefits, and barriers to adherence. Behavioral skills refer to the practical abilities and strategies that individuals need to adhere to their treatment regimen. The main premise of the IMBS is that information, social, and personal motivation to change coupled with perceived and objective behavioral skills lead to adherence behavior.

METHODS

Study design and participants

We conducted a convergent parallel mixed-methods study.[17, 18] The convergent parallel design incorporated the concurrent collection, analysis, and interpretation of qualitative and quantitative data. The findings were then compared and integrated to offer a comprehensive understanding of TKI adherence. This design facilitate a more nuanced and detailed investigation of adherence patterns among these patients.[19] The quantitative data describe their knowledge level, side effects, stress, emotional support, and self-efficacy. The qualitative data capture unanticipated facets of the factors influencing their TKI adherence, uncovering the rationale and experiences behind the numbers, which aid in interpreting the quantitative data. The study was approved by the Institutional Review Board (IRB) of the study site.

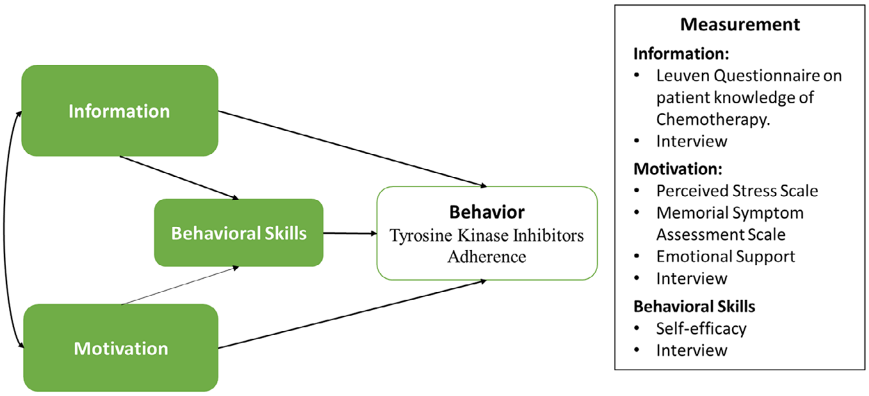
All the participants were English-speaking, men and women aged 18 or older who were diagnosed with CML, had current or past treatment with a TKI, and resided in rural South Carolina. Rurality was determined using the Rural Health Information Hub, Am I Rural?—Tool.[20] Individuals were excluded for the following: institutionalized or had cognitive impairment as noted on their electronic medical record or during the recruitment phone call. All the participants traveled to an oncology clinic in an urban setting for care.

Procedure

After obtaining an IRB waiver, the Principal Investigator (SH) screened records from a large Southeastern outpatient oncology practice for eligible rural patients. Only those patients that fit the rurality criteria were recruited.[20] Recruitment followed an established protocol,[21–24] involving personalized letters and brochures, followed by phone calls from trained race-concordant recruiters. The recruiter, using a script, gave an overview of the study and answered questions. Additional contacts were made to give the individual adequate time to decide about the study. If the participant did not respond to calls, a second recruitment letter was sent.

If the individual agreed to participate, the assessor scheduled a telephone appointment for the consent and first assessment meeting, due to COVID 19 restrictions. During the appointment, the assessor reviewed the study details and obtained informed verbal consent, including an authorization to review medical records. The consent procedure was documented, and a copy of the consent was mailed to the participant. Data were collected from March 2020 to December 2020.

FIGURE 1 The information motivation and behavioral skills model with measures.



Quantitative data collection

Quantitative data were collected on the following variables: demographic information, patient information on CML, perceived stress, side effects, emotional support, and self-efficacy for managing chronic condition. Figure 1 illustrates the study measures guided by the IMBS.

Demographic information

This demographic scale was adapted from previous studies.[22, 25, 26] We collected information on socio-demographic characteristics including age, marital status, occupation, education, and income and medical factors including name of TKI and length of treatment.

Patient information on CML

Patient information was measured using the revised Leuven Questionnaire on Patient Knowledge of Chemotherapy (L-PaKC).[27] This instrument, revised with permission for CML treatment with a TKI, assesses patient treatment knowledge with six multiple choice items. The content validity of L-PaKC is good (CVI = 0.78–1.00).[27] The adaptation was originally for breast cancer and included changes for a low literacy sample.[28, 29]

Perceived stress

The National Institutes of Health toolbox Perceived Stress Scale (PSS) was used to assess the participants' subjective stress experience.[30] The PSS contains 10 items, with response categories ranging from never (1) to very often (5). Aggregate sums were determined for each participant and a mean of the aggregate sums was calculated for the participant group. A larger number indicates a higher stress level.

Side effects

The Memorial Symptom Assessment scale was used to measure side effects, including measures of a diverse group of common symptoms experienced by the participant in the past seven days.[31] A total of 32 symptoms were included in this questionnaire. Each symptom was evaluated for frequency, severity, and distress. Each symptom was recorded as present or absent, and based on the participants' answer, a four-point rating scale (1–4) was used to assess frequency and severity, and a five-point scale (0–4) was used to measure distress. A higher score indicates a greater frequency, intensity, and distress.

Emotional support

One type of motivation to adhere according to the IMBS model is perceived emotional support. To assess motivation, we used the Emotional Support Scale from the Patient-Reported Outcomes Measurement Information System (PROMIS).[32] This four-item scale measures the participants' perception of being cared for and valued as a person. Each item uses a 5-point Likert-type response with possible responses of Never, Rarely, Sometimes, Often, and Always. Each question scores from one (never) to five (always); a higher the score reflects a higher level of emotional support. Raw scores are converted to *T*-scores before analysis.

Self-efficacy

Self-efficacy is an adherence behavioral skill according to the IMBS Model. Participants' self-efficacy level was measured with the Self-Efficacy for Managing Chronic Conditions (SE) 8 item short form from PROMIS.[33–35] The SE assesses an individual's self-reported level of confidence in performing specific tasks or behaviors related to medications and treatment in routine chronic illness management. The individual responded to the questions on a 5-point Likert scale ranging from one (I am not at all confident) to five (I am very confident). The total self-efficacy score ranges from 8 to 40; a higher score indicates a higher level of self-efficacy.

Quantitative data analysis

IBM Statistical Package for Social Sciences (Version 29.0) was used for data analysis. We used descriptive statistics-means, standard deviations, ranges, frequencies, and percentages as appropriate.

Qualitative data collection and analysis

After quantitative data collection, the assessor used an open-ended interview to obtain qualitative data. We asked about the participant's experience with CML, adherence issues, and behavioral skills for adherence, their use of adherence skills, and side effect management. Sample questions included: "Tell me a little about your diagnosis and cancer story"; "What did your doctor tell you about your medicine?"; "What are the reasons you take your tyrosine kinase inhibitor?"

The data analysis team consists of two researchers trained in qualitative methods, a clinical nurse with extensive experience working with cancer survivors, and a graduate student with qualitative research training. The investigators used the Clarke and Braun's six-step thematic approach to analyze the data from the interviews.[36, 37] Steps include (1) data familiarization through iterative readings of transcribed interviews; (2) initial coding; (3) searching for themes; (4) reviewing themes; (5) defining and naming themes; and (6) writing the analysis. More specifically, to familiarize and assure accuracy, we listened to the digital recordings and concurrently read the transcripts to begin the iterative process of developing themes. We began this process with the first interview and continued throughout all interviews using line-by-line coding, while we listened and read, we created memos on initial impressions, re-reading, and coding concepts. Codes were categorized through a flexible interpretive approach, constantly considering the variety of ways perspectives and conceptualizations of each concept. As patterns were identified, we described the nature of recurrent themes and their relationship to each other. Finally, we named the themes (as a means of illustrating their essence) and illustrated them with direct quotes.[38, 39] To assure rigor, the investigators separately analyzed the data and compared their findings at each phase of the process and reached agreement on the analysis to assure the dependability of the findings. Further, thick descriptions were used to establish transferability. Detailed notes and file versions were maintained for the audit trail to further assure confirmability.

RESULTS

Quantitative study results

Sample characteristics

We enrolled 16 participants between March and December 2020 whose age ranged from 26 years old to 76 years (mean ± standard deviation [SD], 55.63 ± 15.38). Participants reported taking TKI therapy between less than a year to 12 years (5.56 ± 4.08) and taking between none to up to 14 additional medications (4.94 ±4.37). Fifty-six percent of the sample reported using multiple pharmacies for prescriptions. See Table 1 for detailed demographic information.

TABLE 1 Demographics of rural patient with chronic myeloid leukemia ($N = 16$).

Characteristic	N (%) [a]
Total	16 (100.0)
Gender	
Male	7 (43.8)
Female	9 (56.3)
Race	
White	10 (62.5)
Black	6 (37.5)
Age group (years)	
<45	4 (25.0)
45–65	8 (50.0)
>65	4 (25.0)
Marital status	
Single/divorced/separated/widowed	7 (43.8)
Married	9 (56.3)
p Value	
Income[b]	
<\$20,000	2 (15.4)
\$20,000–\$49,999	6 (46.2)
≥\$50,000	5 (38.5)
Education	
≤High school	6 (37.5)
>High school	10 (62.5)
Multipharmacy	
Yes	9 (56.3)
No	7 (43.8)
Factors related to tyrosine kinase inhibitors adherence (continuous variables)	
	Mean (standard deviation)
Duration of TKI therapy	5.56 (4.08)
Knowledge of Tyrosine kinase inhibitors treatment	14.25 (4.06)
Perceived Stress	26.99 (6.74)
Emotional Support	52.56 (8.33)
Self-efficacy	48.62 (8.26)

[a] Some categories are greater than 100% because of rounding.

[b] Two participants choose not to answer; one reported do not know; percentages are based on those who did answer.

Factors related to TKIs adherence in patients with CML

All participants completed the assessment for knowledge and stress. Thirteen out of 16 participants completed symptom assessment scale related to side effects, emotional support, and self-efficacy scale. Table 1 presents the mean score with standard deviation of various

TABLE 2 Rural chronic myeloid leukemia patients' knowledge of tyrosine kinase inhibitors treatment (*N* = 16).

	N (%)
Knowing the purpose of taking TKI	
Yes, "The oral treatment treats and controls my CML"	16 (100)
Knowing the planned length of treatment	
Yes, "For the rest of my life"	11 (69)
Understanding reasons of blood test prior to oral treatment or getting the medication refilled	
Yes, "Looking if the treatment is working; Checking on my white blood cells, red blood cells and platelets; Check on my blood (i.e., PCR) level to see if the treatment is working"	10 (62)
Knowing what actions might help during treatment	
Yes	13(81)

TABLE 3 Top five reported symptoms and by frequency, intensity, and distress (*N* = 13).

Commonality	*n* (%)	Frequency	Mean	Intensity	Mean	Distress	Mean
Pain	11 (85%)	Difficulty sleeping	3.0	Difficulty sleeping	3.0	Difficulty sleeping	2.2
Lack of energy	11 (85%)	Problem with urination	3.0	Lack of energy	2.7	Feeling nervous	2.0
Numbness/tingling in hands/feet	9 (69%)	Dry mouth	2.8	Dry mouth	2.4	Worrying	2.0
Feeling drowsy, Feeling sad, Feeling irritable [a]	7 (54%)	Lack of energy	2.7	Problems with urination	2.3	Pain	1.9
		Lack of appetite	2.7	worrying	2.3	Feeling irritable	1.9

Note: Commonality: how many numbers of participant reported having the symptoms.
Frequency: how often participants experience reported symptoms (1 to 4; 1, rarely; 2, occasionally; 3, frequently; 4, almost consistently).
Intensity: the severity of the side effects among affected individuals (1 to 4; 1, slight; 2, moderate; 3, severe; 4, very severe)
Distress: the level of distress or bother caused by the reported side effects among affected individuals (0 to 5; 0, not at all; 1, a little bit; 2, somewhat; 3, quite a bit; 5, very much).
[a] The same number of participants reported experiencing three symptoms: feeling drowsy, feeling sad, and feeling irritable.

related factors. Table 2 presents the CML Patients' Knowledge of diagnosis and treatment of TKIs. Table 3 presents the top five reported side effects.

Qualitative study results

All 16 participants completed the interview, which last between 30 and 120 min. The characteristics and factors potentially associated with TKIs adherence are presented in Table 4. There were five themes derived from the results in terms of CML experience and adherence to TKIs.

Theme 1: "Out of nowhere"

According to Fisher and colleague's IMBS Model of adherence, knowledge about the disease and treatment begins the process of adherence. Our participants' knowledge of their disease was often acquired abruptly through a routine blood test and was a shock to them. In one instance a hairdresser's observation about hair loss led to the diagnosis of CML. Most participants did not feel sick but may have experienced fatigue.

After being referred to an oncologist and having a bone marrow biopsy the oncologist said, "you have CML" and I was like ''what's that? and he "chronic myeloid leukemia." (ID 16)

I went to the hospital to get eye surgery and they told me they could not put me to sleep because I had leukemia. (ID 1)

Theme 2: Knowledge of CML and treatment

Subtheme 2.1. "Cancer cells at bay."

After confirming their diagnosis, most participants acquired only basic information about CML, with some specific knowledge about the purpose of the blood test and TKI treatment.

Medication takes it for the rest of my life but that it had shown and proven to be really effective with patients that had CML and

TABLE 4 Characteristics, length of diagnosis, stress, emotional support, and self-efficacy of interviewed participants ($N = 16$).

ID	Age, year	Gender	Race	Length of taking TKIs, y	Knowledge	Stress	Emotional support	Self-efficacy
1	56	M	W	7	17	25	-	-
2	58	F	W	7	13	32	-	-
3	34	F	W	8	17	35	49.0	48.20
4	49	F	B	3	10	33	43.7	32.76
5	26	F	W	0	16	36	62.0	46.56
6	43	M	B	0	15	34	62.0	60.74
7	71	M	B	6	12	33	49.0	38.30
8	76	F	W	2	19	34	45.4	39.15
9	74	F	W	8	11	32	62.0	54.95
10	65	M	W	13	8	22	53.0	46.56
11	59	F	W	0	21	31	62.0	49.91
12	64	M	W	4	15	35	42.1	52.15
13	76	F	B	14	18	32	49.0	49.94
14	36	M	W	2	18	31	-	-
15	51	M	B	4	8	26	42.1	52.15
16	52	F	B	1	10	32	62.0	60.74

Note: Knowledge and stress were reported sum score. Emotional support and self-efficacy were reported *T* score.
Abbreviations: F, female; M, male; B, Black; W, White; TKI, tyrosine kinase inhibitors.

helping their blood counts come down [and] return to normal levels and really helping patients with CML lead more normal lives. (ID 4)

Keeps the cancer cells at bay or it kind of levels out the CML; a number they are watching; that is what it's supposed to be controlling and it kills those whatever it is supposed to. (ID 5)

Subtheme 2.2. CML patients' understanding of treatment

In contrast to very basic information about their disease, participants had both general and detailed understanding of their treatment, often naming the drug, the drug class (immunotherapy or TKI) and changes in drug regimen. Only two participants supplemented their knowledge about their treatment by searching online or joining online CML support groups. Most participants described a teaching session about their treatment from a nurse educator in the physician practice. The participants seemed to find the teaching sessions very helpful with one exception.

They talked to me and told me it was going to be an oral chemotherapy and I went to a class on that. (ID 10)

She took me and my husband into her office and we discussed all, all the possibilities of the side effects. (ID 11)

Didn't really inform me too much about anything necessarily other than reading what I could have read myself on the back of the prescription bottle. (ID 12)

Theme 3. Various side effects impact on daily activities

Participants reported experiencing various side effects after taking TKIs. Notably, some of these side effects significantly impacted their daily activities.

I could hardly walk from my car to the door to go into the office. My legs hurt that bad; to smell the food, to smell the cologne, oh my God, it was terrible. (ID 13)

No one knew I was going to turn out to be allergic to it. It took me four months to get over one pill. [another oncologist] put [me] on steroids. As soon as the steroids wore off, I was right back on the couch and no energy, could not do nothing. Then I started breaking out in welts for about three months and I finally got used to the medicine. [But I] was not in remission, [the oncologist] doubled the medicine, and [I took] it for two or three months and woke up and was swollen up from my waist up. My hands would be three times the size. (ID 1)

Heart race [on high does original course of treatment]; severe headaches; nauseated all the time. I feel totally sick. I cannot even get out of bed I'm so sick. (ID 16)

Theme 4. Motivations for adherence

Subtheme 4.1 Keeping my leukemia in remission

Staying in remission is a central focus for participants, who prioritize daily adherence to mitigate health risks. Their gratitude extends to each day post-diagnosis, as medications prolong their time, enabling them to be present for their loved ones.

I always take it every day because I don't want to not take it and then something happens. (ID 6)

It is to keep my leukemia in remission. My husband and my family because I want to be here for them. My little great-grandson that just come in here and said "good morning. I love you. See you later." Support, family support; Faith, having faith; Family support and don't push people away that love you. (ID 2)

It's because I didn't want to die at 31. Something we read that [without TKI] when patients got diagnosed the life expectancy was like 3 years. So, I mean technically I'm kind of on borrowed time if it wasn't for medicine. My family and my little daughter had just turned 2 at the time. So, I remember she was young and didn't really know what was happening, but you know could kind of tell that I was sick you know when she would come see me at the hospital those few days that she did. We had tons of visitors from church, the community, work, tons of emails, texts, carrier pigeons, smoke signals, any of that stuff. (ID 14)

Subtheme 4.2 Social supports from friends and families

The experiences shared by these individuals highlight the profound impact of support networks during their journey with CML. The role of companionship, faith, and social bonds helped the participants in navigating the challenges proposed by CML.

I have a friend. She is a retired nurse… She was so faithful to bring me food and text me. She was wonderful. She is really the only one… of course my sister would bring me some food sometimes because she loves to cook. I sort of felt like it was a death sentence initially but then I turned to my faith and to the word that I knew and comforted myself and talked to myself and strengthened myself in the Lord. (ID 8)

I'm really close with my family and friends, so I mean sometimes I fall off the boat and it's like well I haven't taken my medicine today or something and they are very good about saying no you need to take it. I will call you at 7 o'clock in the morning and make sure you are taking it. My friends and family are very supportive. (ID 5)

Theme 5. Strategies used by patients' adherence to TKI

In the study, participants devised a variety of strategies to ensure adherence to their TKI regimen. These strategies included the use of reminders and the maintenance of a consistent schedule. Alarm systems were employed to aid in remembering to take medication at the appropriate times. Alternatively, some participants opted to take their medication at the same time each day, thereby establishing a routine and minimizing the risk of missed doses. Furthermore, participants reported experiencing physical symptoms, such as joint pain, when their TKIs were not taken on time. These physical manifestations served as tangible reminders and provided additional motivation to adhere to their medication schedule. Despite these strategies, participants encountered obstacles in maintaining their TKI therapy. A notable challenge was the process of refilling their TKI prescription, which could introduce logistical complications.

I used my phone alarm to take my medicine to make sure that I would take especially the Tasigna (Nilotinib) that I had to take every 12 h. (ID 13)

It just becomes a habit. More so when I get up in the morning. I started taking it at the same time. But, as the day progresses, if I don't take it within a certain amount of hours, I start to feel some pain so that is the reminder. [I] need to take it because otherwise I will get nauseous or start having joint pains. (ID 6)

They gave me a prescription where I had to travel out on Long Island to the only pharmacy in that area to get it. Even [when I] moved to South Carolina, I drove back once a month to get the prescriptions. And then eventually I was able to get it transferred to South Carolina. I was getting it through my insurance at first. When I moved to South Carolina, I was unable to transfer my insurance. So, I was able to get the Patient's Assistance program, which furnished the medication and I stayed on that until I turned 62. Then, I started drawing my Social Security [and received Medicare coverage]. (ID 7)

DISCUSSION

Adherence is a crucial factor affecting the effectiveness of CML treatment. TKIs are considered one of the most successful classes of targeted therapies developed in cancer. We captured qualitative and quantitative data on patient-specific, medical, and psychosocial factors influencing TKIs adherence in rural adults diagnosed with CML. Understanding of rural patients' TKI adherence behaviors based on a theoretical framework enhances the possibility of developing successful interventions tailored for these individuals.[40] Interviews identified key behavioral determinants based on the IMBS leading to adherence to TKI therapy. Dominant IMBS concepts ("knowledge," "motivation," and "behavioral skills") are essential to the development of interventions and strategies to enhance TKI adherence.

Our survey findings highlighted a concerning inadequacy in patient knowledge regarding CML treatment. This shortfall became apparent during interviews, which provided greater depth and further elucidated the survey results indicating a poor understanding of the duration of TKI therapy and the purpose of regular blood tests. This deficiency in knowledge may stem from the initial time of diagnosis; participants reported being blindsided by their CML diagnosis, potentially leaving them with little opportunity to process the information and understand the treatment plan. Most participants reported receiving only elementary information about CML. This lack of comprehensive education and processing time can lead to misconceptions about treatment management—for instance, some participants were unaware of the lifelong necessity of TKI therapy. The authors recognize that in some cases, TKI therapy may be stopped completely.[41] Previous evidence showed educational efforts and regular monitoring are pivotal in enhancing TKI adherence.[42] Our findings underscore the critical need for a standardized protocol that considers the time from diagnosis and increased frequency of education sessions to inform patients effectively and provide them with adequate education in clinical settings. Due to the chronic nature of CML, the necessity for daily dosing, and the extended treatment period, future research should further examine adherence within the context of living with CML using Transitions Theory.[43]

In the context of IMBS, "Motivation" is a multifaceted construct encompassing both personal and social dimensions. Personal motivation is characterized by an individual's emotions and attitudes—positive or negative—toward adherence, the perceived benefits of maintaining consistent therapy, and the anticipated adverse consequences of nonadherence. Conversely, social motivation is shaped by the perceived social support for adherence and the individual's inclination to conform to the expectations of others. A salient barrier to adherence identified in our study is the side effects associated with treatment. Our research revealed that the side effects most commonly encountered by participants did not always align with those that were the most severe, distressing, or frequent among individuals. Notably, while pain was frequently cited as a side effect, insomnia emerged as the most severe and distressing for those affected. This discrepancy underscores that certain side effects, albeit less prevalent, exert a disproportionate impact on the quality of life for individuals with CML. These insights compel health care providers to contemplate targeted interventions for the less common, yet more consequential side effects, such as difficulty sleeping. Tailoring support to these specific challenges holds promise for enhancing TKI therapy adherence among rural CML patients.

Our findings further indicate beneficial factors influencing adherence predominately operate at the individual and group level, such as stress and side effects management. The literature corroborates this focus on the individual.[40] Existing strategies include the provision of educational information and guidance by health care professionals, the encouragement of support through the use of adherence aids or regular contact to reinforce behavior change, and coaching to encourage self-management of symptom and medication.[40] However, a notable challenge from our study was the process of refilling their TKI prescriptions, which could introduce logistical complications. This highlights the imperative for systemic enhancements in adherence practices, particularly at the community or structural levels, to facilitate access to TKI prescriptions. Therefore, our study underscores the importance of multilevel strategies in enhancing TKI adherence among rural CML patients, providing evidence for improved patient outcomes and a more comprehensive understanding of treatment adherence in real-world settings.

TKIs are a cornerstone of targeted therapy for CML. However, since TKIs are taken orally, patients carry the burden of implementation. It is critical to instruct and improve their self-management skills in implementing TKIs. Given the protracted nature of CML treatment, the daily dosing requirement, and the long-term commitment to therapy, sustaining adherence is a formidable challenge. Despite good adherence to TKIs resulting in a significant increase in CML patients' survival rates, with the possibility of nearly full life spans, researchers continue to document a low adherence rate.[44] Previous evidence suggested that interventions aimed at improving patients' levels of adherence should take into account each patient's circumstances, including the use of reminders and routine symptom assessment and management as components of a comprehensive intervention strategy.[45] These findings are consistent with our research. Our findings advocate for patient-centric educational initiatives that focus on adherence skills. Such personalized instruction is posited to significantly bolster adherence to TKI therapy among CML patients. The evidence suggests that when patients are equipped with the knowledge and tools to manage their treatment effectively, adherence rates improve, thereby optimizing therapeutic outcomes.

Limitations

While the mixed-method approach and the use of a theoretical framework are study strengths, our study has limitations. The small sample size, partly due to COVID-19 and rural criteria, precluded comparative and correlation analysis. However, our primary aim was to descriptive analysis rather than to examine the association between variables. Also, only 13% of CML patients are rural dwellers, according to the Surveillance, Epidemiology, and End Results 19 registries database.[46] Future research should evaluate factors related to TKIs adherence and to understand how these factors correlate. Secondly, our study participants reported being adherent to TKIs, but adherence was not directly measured. We recommend that future research should consider using objective measures, such as medication tracker bottles and blood tests, to assess TKIs adherence rate more accurately. Lastly, our single-state sample limits generalizability, necessitating boarder multistate studies.

CONCLUSION

This research uncovers the complexities and driving forces influencing TKI adherence among rural CML patients. Our findings underscore the need for heightened focus on adherence strategies to realize the objectives of CML treatment. Given that this was an observational, descriptive study carried out in a real-world context, our findings could contribute valuable insights for the formulation of strategies aimed at enhancing TKI adherence. We identified several influencers, including the navigation of the diagnostic process, the impact of the disease or its treatment, professional and social support, and knowledge of CML and TKI treatment. Future investigations should quantify the impact of these factors to better understand and address adherence challenges in rural CML patient care.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose.

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