Challenges to Care and Medication Adherence of Patients With Chronic Myeloid Leukemia in a Resource Limited Setting: A Qualitative Study

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Abstract
The factors related to care of patients with chronic myeloid leukemia (CML) often affects treatment outcome. We examined adherence to medication and other challenges to care in our patients on treatment of CML. This qualitative study involved in-depth interviews of 20 patients with CML receiving free imatinib (Glivec) from the Glivec International Patients’ Assistance Program. Data collected were thematically analyzed. Findings revealed that despite free drug assistance, there was relative lack of awareness resulting in inappropriate health-seeking behavior. The challenges cut across situations such as poverty, fear of the sustenance of the compassionate drug program, and living far away from the clinic. Forgetfulness was reported as the cause of poor adherence in this study. Suggested solutions include increasing community awareness, ensuring sustainability of the program and establishing more treatment centers nationwide. Strategies such as reminders and patents’ support will improve drug adherence among this cohort.

Keywords
drug adherence, CML patients, challenges to care

Introduction
Chronic myeloid leukemia (CML) is a hematological malignancy affecting all age groups albeit diagnosed in advanced stage in developing countries therefore leaving only care available as palliative or end-of-life care (1). However, with the introduction of imatinib, a breakpoint cluster region-abelson gene tyrosine kinase inhibitor, an anticancer agent known to significantly improve clinical outcome and reduce morbidity and mortality in these patients, their quality of life has been reported in various studies to increase markedly (1–3). This makes this drug a first-line therapy among other tyrosine kinase inhibitors (4). However, to ensure quality and durable remission, it is necessary to emphasize adherence to this drug and prevent cancer progression (1,2). Good adherence of patients with CML to imatinib showed remissions at critical time lines with poor adherence resulting in delayed or no remission with potential imatinib resistance (3,5).

Previous studies on the factors responsible for poor adherence identified patient-related factors, treatment-related factors, and health facility factors. Patient-related factors include age, gender, availability of treatment support, and stage at diagnosis; treatment-related factors include knowledge of disease and its treatment and cost and frequency of dosing; and health facility factors include

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health workers’ factors, waiting time, and distance from clinic (1,3,5).

In resource-limited settings such as Nigeria with relatively low-level personnel and facilities for oncology management, diagnosis of cancer including CML is regarded a death sentence with little or no treatment available since cancer drugs have to be imported hence often time out of reach of patients due to high cost (6). This study evaluates delayed diagnosis, health-seeking behavior, medication usage, and other challenges to care of people living with CML on imatinib in Ile-Ife, Nigeria.

Methods

Study Setting

This qualitative study was undertaken from April to May 2016 at the Hematology Clinic of Obafemi Awolowo University Teaching Hospitals’ Complex (OAUTHC), Ile-Ife, Nigeria. The Glivec International Patient Assistance Program (GiPAP) commenced in OAUTHC since June 2003 and remains the only center in Nigeria providing free imatinib (Glivec, Novartis International AG, Basel, Switzerland) to patients with CML. The over 1000 diagnosed patients have a median age of 36 years, with a male to female ratio of 1:1.5, less than 15% had below secondary education, and most were traders and artisans with 18% working in civil service (7). The patients are seen routinely on clinic days (Tuesday and Thursdays) for disease confirmation, commencement of imatinib, and follow-up. In cases of emergencies, they are seen or admitted to the medical wards through the hematology day care unit or the accident and emergency unit of the hospital. The clinic is staffed by a team of consultant hematologists and resident doctors, nurses, pharmacists, and other support staff with requisite training. These staff routinely counsel the patients at presentation on the disease, its treatment, timing, and adherence. Adherence counselling is received from these health workers at each consultation. Nurses trained on adherence do adherence counselling for new patients accessing drugs. Also, patient support group meets regularly and is headed by a patient of long standing in the program who has been trained on advocacy and adherence counselling skills. Patients are seen at initial presentation, 1 month and thereafter 3 monthly for drug refills, adherence counselling, and follow-up. During industrial action involving doctors or other health workers, special arrangement is made by the management to ensure continuous care to these patients.

Study Participants

Twenty patients diagnosed with CML who had been on Glivec for over 1 year were purposively selected from the list available in our record department at the monthly interaction and support meeting of the patients with CML (Table 1). This selection was done to reflect the different 6 geopolitical zones of Nigeria comprising of the South West, South South, South East, North West, North East, and North Central.

| Variable                      | Frequency | %  |
|-------------------------------|-----------|----|
| Age (years)                   |           |    |
| 20-39                         | 8         | 40 |
| 40-60                         | 12        | 60 |
| Sex                           |           |    |
| Male                          | 10        | 50 |
| Female                        | 10        | 50 |
| Marital status                |           |    |
| Single                        | 3         | 15 |
| Married                       | 12        | 60 |
| Widow                         | 3         | 15 |
| Divorced                      | 2         | 10 |
| Level of education            |           |    |
| Primary                       | 2         | 10 |
| Secondary                     | 10        | 50 |
| Tertiary                      | 8         | 40 |
| Occupation                    |           |    |
| None                          | 1         | 5  |
| Trading                       | 14        | 70 |
| Civil servant                 | 4         | 20 |
| Artisan                       | 1         | 5  |
| Ethnic group                  |           |    |
| Yoruba                        | 9         | 45 |
| Ibo                           | 4         | 20 |
| Hausa/Fulani                  | 2         | 10 |
| Others                        | 5         | 25 |
| Geopolitical zone             |           |    |
| North West                    | 2         | 10 |
| North East                    | 1         | 5  |
| North Central                 | 4         | 20 |
| South West                    | 8         | 40 |
| South East                    | 3         | 15 |
| South South                   | 2         | 10 |
| Duration of clinical diagnosis (years) |   |    |
| 2-7                           | 19        | 95 |
| >7                            | 1         | 5  |
| Level of drug adherence       |           |    |
| Ever missed                   | 1         | 5  |
| Never missed                  | 19        | 95 |

*Refers to other ethnic groups.

Ethical approval was obtained from the institutional ethics and research committee, while consent was taken from each participant at enrollment. The in-depth interviews were conducted by the authors using an instrument developed from the study objectives and the literature review.

There were 10 male and 10 female participants, age ranging from 24 to 56 years, with 2 (10%) having primary education, 10 (50%) had secondary education, and the rest (40%) had tertiary education. Twelve (30%) were married, 3 (15%) were single, 3 (15%) were widowed, and 2 (10%) were divorced. One (5%) participant was unemployed, 14 (70%) were trading, 4 (20%) worked in civil service, and 1 (5%) was in catering business. There were 9 (45%) Yoruba, 4 (20%) Igbo, 1 (5%) Tiv, 1 (5%) Ijaw, 3 (15%) Edo, and 2 (10%) Hausa. The respondents’ place of residence were spread across the 6 geopolitical zones of Nigeria from Kano to Bayelsa, Port Harcourt to Zaria, and Lagos to Sokoto.
One respondent has been diagnosed and commenced on imatinib for 11 years, while the rest were diagnosed between 2 and 7 years. Only 1 participant reported ever missed imatinib (Table 1).

Data Collection

In-depth semstructured individual interviews conducted after receiving informed consent were recorded and then transcribed. The interview was conducted in English or Yoruba based on the preference of each respondent. Interviews conducted in Yoruba were translated to English before the data were analyzed. The interview included introductory and demographic questions, followed by open-ended questions aimed at understanding the challenges to care and drug adherence faced by the respondent since commencement of imatinib.

The interview topics include time of diagnosis, where they seek health care before presentation, who referred them and amount spent on care. Other information include experiences since coming to this hospital, opinion on social health insurance, and challenges faced since diagnosis. The respondents were asked to discuss these challenges and whether or not they have overcome them. They were asked to suggest solutions to these challenges. They were requested to specify other important information that they wish to add. The interviews were conducted in area acceptable to the respondents to ensure confidentiality and lasted about 45 minutes.

Data Analysis

A rapid analysis of the field notes was done first to identify major pattern and preliminary themes. Interviews were transcribed and transcripts edited for accuracy. Themes were developed in line with study objectives. Grounded theory approach was used till saturation was reached. Content analysis of thematic areas was thereafter done.

Results

Health-Seeking Behavior Before Diagnosis

Many visited and were admitted in various hospitals before referral to our hospital. Some were misdiagnosed in these hospitals leading to their late presentation. Many spent a significant part of their family income during this period. Some used herbal drugs worth about 18 000 Naira (about US$50) without improvement. This period ranged from 6 months to 1 year. Another respondent asserted:

When I fell ill, I was admitted in several hospitals with different diagnoses. I received different treatments and herbal drugs with little or no relief. I was eventually taken to Federal Medical Center from where I was referred here. (45-year-old male civil servant).

One woman did not spend much as she presented early. Other respondents spend between 100 000 and 5 000 000 naira (US$250-US$13 000) before presentation. A respondent went as far as United Kingdom where she was diagnosed and referred to our hospital.

The respondent stated:

I was very ill, I could not stand and I have no blood that my husband took me to several hospitals and herbalist homes with no relief. He spent over a million naira (2500 US dollars) to get me well but my condition did not get better. I was flown abroad from where I was referred here (52-year-old caterer).

Drug Issues, Adherence, Adverse Effects, and Treatment Support

Factors affecting drug adherence among these respondents include patient-related factors, health facility factors, and drug-related factors. Although only 1 respondent reported forgetfulness as the reason for missing the drug, they felt that their drug adherence could be better if they do not have to travel far distance to the health facility. Also, side effects could be responsible for inadequate drug adherence. For instance, the participants believe that side effects such as low blood level, abdominal pain, vomiting, depression, weakness, dark menstrual flow, poor penile erection, and sexual dysfunction could result in poor drug adherence. However, only 2 participants have experienced some of these side effects which they described as mild and quickly managed by their doctors hence did not lead to poor drug adherence. No participant reported any negative effect on sexual life or penile erection.

Generally, the respondents believe that the drug has a strong positive effect that improved their quality of life. One respondent said:

We are told to take the drug with water but never to take it with apple and other fruits. Taking the drug have stop frequently ill-health (56-year-old surveyor).

Also, some participants use herbal preparation meant for other complaints with the drug and have not experienced any side effect. Some patients take herbal drugs for other ailments but none take it for the disease. They believe that herbal drug/tea/bitters do not interact with their drugs. One respondent stated:

I used yoyo bitters with my drugs, it makes me feel good. (43-year-old female trader).

Everyone was happy that the drug is provided free and that has improved the quality of their life since they started it. They were also happy that they had never experienced stock out even during workers’ strikes. Another respondent said:

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It is good that I have done well with the drug, the drug is good for me, I have never missed taking it as my Doctor make sure I get it even during Doctor’s strike, he also calls me to find out how I am doing. (42-year-old female trader).
The good drug adherence reported despite several limitations among the respondents is due to their relationship with their caregivers, especially the doctors. They have access to the doctors' phone numbers which when they call, and the doctors always call them back. They call their doctor at any time sometimes in the night. They felt the present situation of doctors prescribing more than 1 month drug is very good especially to patients from far places. This they felt is mainly responsible for their good drug adherence. Only 1 respondent has reportedly missed taking the drugs since he started it. He said that he forgot it at home when he travelled. They agreed that their family members assisted them in not forgetting their drugs. Some participants set their phone to remind them. The drugs are well kept by these participants.

A respondent said:

My drugs are kept in its pack and away from my children. My husband reminds me to take my drug, at times my phone ring when it gets to the time to take it, I have never missed it (35-year-old trader).

Another respondent said:

I come from Kaduna State to collect my drugs; I learnt other people come as far as Bayelsa State to pick their drugs at this hospital. I collect my drugs free. The health workers are very nice as they ensure we are always with the drugs and call us to find out about our welfare, God will be with them. (44-year-old trader).

One factor affecting drug adherence includes rising laboratory cost which is necessary to monitor their treatment. They stated that the laboratory tests are becoming more expensive and beyond the reach of some patients. Some tests results are not available when needed for patient monitoring. A respondent said:

Although the drug is free, the laboratory tests are becoming too costly with some tests not available, there is also delay in receiving the results which make the situation a bit difficult for people coming from far places like myself. I came from Abuja. (33-year-old trader).

Influence of Spirituality on Care

The finding that the participants believe in divine healing despite having good adherence could be due to the information, education, and communication given to them by trained health workers at diagnosis and commencement of therapy. These patients are routinely informed about the deadly disease, that it is not a spiritual attack and that continuous use of the drug is the only sure way to combat the disease. They were commenced on the drug after several adherence counselling sessions by trained adherence counsellors/nurses. At every visit, these patients were counselled on drug adherence at every contact. They were ready to continue taking their drugs until their doctors confirmed that they are healed. Some participants take anointed water with the drugs. Some participants were initially taken by their relatives to religious places for fasting and prayers but when there was no improvement, they were brought to the hospital for care. They said they are happy with the treatment received from the hospital. A respondent stated

I believe in divine healing, but my faith failed me as I did not get better with fasting and prayer when I fell ill before coming here. The drug is provided by the holy spirit. I always take it with anointed water. I was very ill and carried to this hospital when I first came and was on admission for months. I am now okay by God’s grace. (43-year-old civil servant).

Satisfaction With Care

Although all participants were satisfied with the care received from the hospital, they were concerned about the sustainability of the program. They stated that doctors were ever ready to respond to their care needs including giving more than 1 month drug package for patients coming from far places and calling them regularly to find out how they are doing on drug therapy. They were happy that they have access to their doctors at any time even in the night. However, 1 participant stated that young doctors need to be educated on patients care as she remembered that she once had a disagreement with one of the younger doctors which have since been resolved. A respondent said:

The doctors are hardworking and friendly to us. They take good care of us. I always pray for them as they are so committed. Imagine, I have been on treatment here for many years but they never joined any strike. They call me about my welfare and refuse to collect anything from me. They are so supportive. I heard they do the same to other patients. Government should take good care of these committed workers. (46-year-old civil servant).

Suggestions to Improve Patient’s Care

This includes having health workers with the disease as their caregiver, also employing some people with the disease who are currently unemployed and reducing the cost of laboratory tests, prompt release of laboratory results, and appropriate referral for other disease conditions.

Some respondents believe increasing the number and spread of hospitals giving the drugs will improve their care and reduce the waiting time at the hospital and that they will not need to travel long distance to pick up their drugs. Other suggestions include the need to employ and train people with the disease as counsellors in the clinic, need for a clinical psychologist, conducive waiting area for patients, need to employ more record attendants, need for more patient convenience/toilet facilities, and need to employ more doctors/other staff to reduce waiting time. They want the laboratory tests issue be looked into urgently as it is becoming more expensive and beyond the reach of some patients. Also, some tests are not available when needed for patient monitoring.
Another respondent said:

I thanked God I am alive. It will be good if I can have this care in my state. I believe people living with the disease who are also on treatment could be trained as counsellor or something and employed so as to reduce unemployment among the patients. Other workers could be employed so that we can be attended to on time. It will be very good if the laboratory cost can be reduced downwards to affordable level and free for patients who cannot pay. (37-year-old female trader).

When asked about their opinion on social health insurance, none have enrolled or see need to enroll in the hospital’s health insurance program.

One respondent stated:

Since the drug is provided free, what will I need health insurance for? Will it take care of my transport money from Kano? I will be wasting money if I enroll in the hospital health insurance (46-year-old male civil servant).

All respondents requested that information given in the clinic suggestion box should be given immediate consideration so as to further improve patients care.

**Discussion**

The baseline qualitative study evaluated the challenges to care and drug adherence of our patients. This study reported inappropriate health-seeking behavior before enrolled into the program. This finding was due to misdiagnosis, low awareness of the disease, and our treatment program by the participants and their family caregivers. Previous studies have shown health-seeking behavior as a cause of delay in presentation (7–10). This implies that since patients usually present at the advanced stage of the disease, treatment becomes difficult with the only care available as palliative and end-of-life care. Although imatinib has revolutionized the care of CML from a deadly disease to a manageable chronic disease, early diagnosis is crucial in its management as patients with early chronic phase CML usually present with low Sokal score with high probability of achieving major molecular remission and possible “cure” of the disease. Studies have reported excellent imatinib response and good clinical outcome when the interval between diagnosis and commencement of treatment is short (11,12). The inappropriate health-seeking behavior of these patients allow wastage of limited funds available to them. MacLachlan et al reported this finding in their study on symptom perception and help-seeking behavior prior to lung and colorectal cancer diagnoses (13). Our respondents seek care in various religious centers and herbal homes looking for spiritual healing hence allowing progression of this deadly disease. Many also visited other hospitals where they were misdiagnosed. By the time they get to the hospital, they had no money available for their care. Hence, the free provision of this life-saving drug increases access to patients with meagre resources.

However, the increase in laboratory cost need to be looked into if the gains of the program must be sustained. Also, there is need for awareness creation on importance of social health insurance so as to mitigate these increasing cost of care such as cost of laboratory test. The delay in getting laboratory results could hinder patients monitoring as it delays decision-making, hence, delaying access to therapy.

The study participants reported good adherence to therapy with only 1 participant ever reporting nonadherence because of forgetfulness. Previous studies reported the need for perfect drug adherence for optimal response to imatinib (1–3,14). Although these participants believe the drug does not interact with herbal therapy and anointed water, it will be good to investigate this assertion as it may not be true. For centuries, herbal preparation had been the main treatment for most diseases including cancer especially in resource-limited countries (15–17). However, herbal therapy and anointed water could contain substances that could interact with the drug given to these patients. This could affect the effectiveness and efficacy of imatinib therapy.

Although the participants expressed fear about the sustainability of this life-saving program, they believe in their physicians and other health workers as they were satisfied with the care received at the hospital. This could partly be responsible for good adherence to therapy. Also, giving more than 1 month drug to patients living far away from the treatment center and constant communication by doctors with the patients also help their adherence to therapy. Also, the use of phones to remind them to take their drugs and family support further improve drug adherence. Patient–physician communication is better when care is patient centered with patient education, continuous adherence counselling leading to improved drug adherence, and treatment outcome (1,17,18). This finding shows the importance of continuous and ongoing counselling at each contact with the patients and regular phone calls by these health workers to find out about the patients’ welfare. Also, the fact that clinic services continue during doctors or other health workers strikes improves care and drug adherence.

Suggestions to improve care include need to employ patients living with CML as counselor in the hospital setting. This will reduce unemployment among the patients and enhance the program. The request for immediate action on information submitted into the clinic’s suggestion box will further improve care accessed by these patients. Also, the request for more GIPAP centers will enable more patients to access imatinib (Glivec) treatment. It will also improve drug adherence as they no longer have to travel long distances to come for drug refills and follow-up. Other suggestions such as need for a clinical psychologist, conducive waiting area for patients, need to employ more record attendants, and need to employ more doctors/other support staff to reduce waiting time will further improve care accessible to these patients.

Although this qualitative study was carried out at the only center where imatinib (Glivec) is available free to patients with CML in Nigeria, this may limit the generalization of its
findings to the entire patients with CML; however, it serves as a baseline for future study.

**Conclusion**

Care of patients with CML in our setting will improve if more efforts are put into ensuring the sustainability and decentralization of the international free drug assistance program. This will increase access to the program. Also, reminders, parents’ support, ongoing counselling will improve drug adherence. More community sensitization and regular training of health-care workers are necessary especially at the primary care level to ensure early diagnosis and prompt referral.

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