

Quality of Life of Chronic Myeloid Leukemia Patients receiving Tyrosine Kinase Inhibitor (TKI): Comparison with Healthy Population

Ajaya Raj Gautam¹, Stuti Bhattarai²

¹Department of Internal Medicine, Rapti Academy of Health Sciences, Ghorahi, Dang, Nepal.

²Research Assistant, Rapti Academy of Health Sciences, Ghorahi, Dang, Nepal.

Article Info:

Received Date: 11 Mar, 2024

Acceptance Date: 8 Jun, 2024

Corresponding Author:

Ajaya Raj Gautam
Lecturer,
Department of Internal Medicine,
Rapti Academy of Health Sciences,
Ghorahi, Dang, Nepal.
Email: ajayaraj15@gmail.com

Funding sources: None

Conflict of interest: None

Access the article online



DOI: doi.org/10.70027/jrahs4

Abstract

Introduction: Development of tyrosine kinase inhibitors (TKIs) has changed the therapeutic landscape of chronic myeloid leukemia (CML) patients with an improved 10 years' survival rate approximately from 20% to 90%. So, Quality of life (QoL) is an aspect of CML disease management that is gaining prominence in recent years. In Patan Hospital also, an increased 10 years' survival rate has been seen among CML patients receiving TKIs under Glivec International Patient Assistance Program (GIPAP). So, the aim of this study was to compare the QoL of CML patients under treatment in Patan Hospital with the apparently healthy population.

Methods: This is a cross sectional comparative study done at Patan Academy of Health Sciences (PAHS) from October 2018 to September 2019. Short Form 36 (SF-36) questionnaire was used for QoL assessment. Ethical approval was obtained. Data analysis was done using epi info version 7.2.2.

Results: Total of 192 participants was included in this study. (98 in each CML group and apparently healthy population). Mean age of the study population was 47.42 years with 33.67% being females. Physical QoL was significantly poor in CML patients. (p value 0.01) but no difference regarding mental QoL between two groups.

Conclusion: Identification of symptom burdens of TKI therapies in routine practice is needed so as to lessen these burdens to effectively improve physical QoL in CML patients. Similarly, for improvement of mental QoL in younger patients (18-39 years' age group), assessment of psychological impact of the disease and proper counseling in these patients is required.

Keywords: Chronic myeloid leukemia, quality of life, tyrosine kinase inhibitors

Introduction

Chronic myeloid leukemia constitutes around 15% of leukemia cases affecting mostly males and age group greater than 70.^{1,2}

CML patients may be asymptomatic or present with symptoms like splenomegaly, fatigue, night sweats, and bleeding.³

Quality of life is an essential aspect in CML management.⁴ Till 2000, drug therapies offered modest survival benefits

but significant toxicities. The use of tyrosine kinase inhibitors improved 10 years' survival of CML patients approximately from 20% to 90%.⁵ However, for this, patients require long-term treatment.^{4,6} Despite mild to moderate side effects, the long-term TKI use could affect the QoL.⁷ Understanding these effects are critical for overall patient care.^{8,9}

Since 2003, Patan Hospital under Glivec International Patient Assistance Program, provides TKIs free of cost

Citation:

Gautam AR, Bhattarai S. Quality of Life of Chronic Myeloid Leukemia Patients receiving Tyrosine Kinase Inhibitor (TKI): Comparison with Healthy Population. *J. Rapti A. Health Sci.* 2024;1(1):11-16.

Copyright:

© Authors retain copyright and grant the journal right of first publication with the work simultaneously licensed under Creative Commons Attribution License CC - BY 4.0

achieving 10 years survival rate of 95%^{10, 11} This study seeks to compare QoL of CML patients under TKI with healthy population to find out the issues hindering QoL in CML patients.

Methods

This study is a single center cross-sectional study conducted in Patan Academy of Health Sciences (PAHS) from October 2018 to September 2019. Approval of the study was obtained from the Institutional Review Committee (IRC) of PAHS. Consent was obtained from all participants. Participants were explained about the study in detail before obtaining the consent. For written consent, generic PAHS format in Nepali was used. If participants wished, they could withdraw at any time without any reasons. We guaranteed confidentiality of all the participants.

CML patients attending CML clinic in Patan Hospital during study period who were >18 years of age with complete hematologic response (CHR) and no self-reported history of other chronic disease like chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, chronic kidney disease (CKD) was included in this study. CHR was defined as White blood cell (WBC) count <10,000/microliter with no immature granulocytes with <5% basophils in differential count, platelets count <4,50,000/microliter and spleen not palpable.

Apparently healthy populations were matched based on age and gender with CML patients included in the study. These study participants were relatives of CML patients attending the CML clinic or relatives of patients admitted to the medical ward of Patan Hospital. They were aged 18 years or older, matched to the patient by gender and within five years of the patient's age, and did not report any chronic conditions such as diabetes mellitus, hypertension, COPD, or CKD. Those who refused to give consent for the study, or those who were <18 years of age or those with history of any chronic disease or those who were pregnant were excluded from this study.

The data regarding the demographic profile of patients was collected from CML patients and age and sex matched apparently healthy populations through structured proforma. Clinical details about CML patients were collected from medical records of Patan Hospital. QoL assessment for two groups was done by short form health survey (SF-36) questionnaire which is a validated questionnaire.¹² SF-36 contained eight scales: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). The SF-36 also provides two summary scores: physical component summary (PCS) and mental component summary (MCS).

Higher scores indicate better QoL. The SF-36 has been shown to be a valid and reliable measure with cancer patients.¹² SF-36 has been used in different QoL studies conducted in Nepal.¹³ SF-36 questionnaire was translated in Nepali language which has been again converted in English language by two different persons. Content and face validation of the questionnaire were done with the help of experts. So, the SF-36 questionnaire in Nepali language was used for data collection. The participants were provided with questionnaires to be filled up by themselves. For illiterate participants, an interview based on the questionnaire was taken and the questionnaire was filled up based on the answers of the participants.

Sample size was calculated using the formula $n_1 = n_2 = (\sigma_1^2 + \sigma_2^2) (Z_{\alpha/2} + Z_{\beta})^2 / (\text{difference in means})^2$. Mean physical component score (PCS), mean mental component score (MCS) and standard deviation in CML population and healthy population was taken from the similar study done by Phillips et al.¹⁴ Confidence interval was taken to be 95%, power of study to be 80% and ratio between 2 groups was taken as 1:1. With this, the minimum sample size in each group was calculated to be 95.

Data were entered in MS Excel 2016 and epi info version 7.2.2 and analysis was done in epi info version 7.2.2 SF-36 domain and summary scores were calculated according to standard scoring guidelines.¹² Normality of data was tested by comparing a histogram of the sample data to a normal probability curve and using Kolmogorov-Smirnov (K-S) test. Comparison of QoL between two groups was done by using independent sample T-tests and Mann-Whitney U test as appropriate. For comparison between more than 2 groups one-way ANOVA test or Kruskal Wallis test as appropriate was used. A P-value of 0.05 or less was considered significant.

Results

Total of 192 participants were included in this study. (98 in each CML group and apparently healthy population group). Out of those, 33(33.67%) were females. Mean age of the study population was 47.42 years. (Table 1) In this study, 66(67.35%) of the CML patients were taking imatinib. (Table 2) Physical QoL as measured by PCS was significantly poor in CML patients. (p-value 0.01) There was no difference regarding mental QoL between two groups as measured by MCS. (Table 3) CML patients of the age group 18-39 years had significantly poor mental QoL. (p-value 0.03). (Table 6) However, there was no difference in QoL outcomes between male and female patients, patients taking different TKIs and patients taking TKIs for different duration (<=1 year, 1-5 years and >5 years)

Table 1: Demographic Characteristics of Study population.

Variables	CML(n=98)	Healthy population(n=98)
Age in years (Mean)	47.71	47.13
Female (%)	33.67	33.67
Literate (%)	60.20	54.08
Married (%)	82.65	80.61

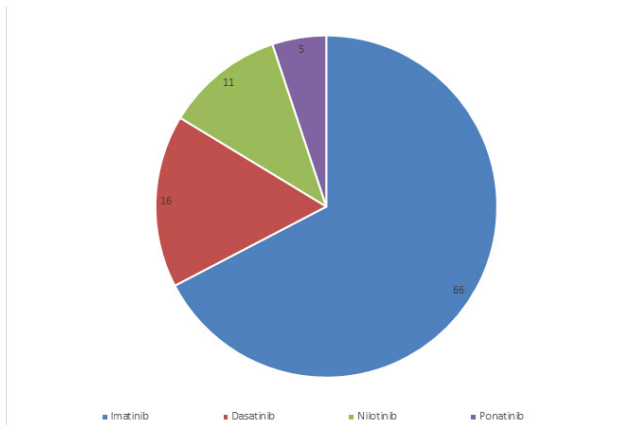


Fig 1: Number of CML patients using different TKIs.

Table 2: Comparison between CML patients and apparently healthy population.

SF-36 variables	CML (mean)	Healthy population (mean)	p-value
Physical health			
Physical functioning	85.26	86.73	0.76
Role physical	71.17	78.01	0.78
Bodily pain	80.66	81.4	0.75
General health	63.55	67.6	0.14
PCS	48.55	50.94	0.01
Mental Health			
Vitality	79.95	71.09	0.96
Role Emotions	69.47	70.61	0.02
Social Functioning	79.04	75.51	0.16
Mental health	72.1	69.08	0.16
MCS	47.71	45.12	0.09

PCS=Physical Component Summary, MCS=Mental Component Summary

Table 3: Comparison of QOL of male and female CML patients.

SF-36 variables	Male(mean)	Female (mean)	p-value
Physical health			
Physical functioning	86.46	82.88	0.24
Role physical	71.92	69.69	0.88
Bodily pain	81.77	78.47	0.46
General health	63.04	64.55	0.72
PCS	48.65	48.35	0.84
Mental Health			
Vitality	69.99	68.42	0.75
Role Emotions	79.50	80.84	0.92
Social Functioning	78.16	80.86	0.63
Mental health	73.48	69.39	0.31
MCS	47.37	48.39	0.67

PCS=Physical Component Summary, MCS=Mental Component Summary

Table 4: Comparison between different age groups of CML patients.

SF-36 variables	18-3 years (mean)	40-59 years (mean)	>=60 years (mean)	p-value
Physical health				
Physical functioning	90.83	85.44	77.61	0.40
Role physical	75.00	75.00	58.70	0.27
Bodily pain	86.18	79.49	75.73	0.29
General health	58.83	65.44	65.98	0.29
PCS	49.87	49.02	45.91	0.10
Mental Health				
Vitality	70.70	70.59	65.65	0.66
Role Emotions	71.12	83.76	84.03	0.35
Social Functioning	80.95	80.89	72.93	0.45
Mental health	70.70	72.02	74.09	0.82
MCS	43.46	48.85	51.03	0.03

PCS=Physical Component Summary, MCS=Mental Component Summary

Table 5: Comparison of CML patients using different TKIs.

SF-36 variables	Imatinib (mean)	Dasatinib (mean)	Nilotinib (mean)	Ponatinib (mean)	p-value
Physical health					
Physical functioning	85.30	82.50	85.46	93.00	0.57
Role physical	71.59	73.44	56.82	90.00	0.26
Bodily pain	80.18	85.50	74.23	85.60	0.61
General health	64.66	63.75	59.55	57.00	0.75
PCS	48.59	48.64	47.37	50.41	0.88
Mental Health					
Vitality	70.22	69.81	61.27	76.40	0.59
Role Emotions	81.32	68.75	81.90	93.40	0.56
Social Functioning	80.57	77.47	70.77	82.10	0.76
Mental health	72.77	74.63	64.36	72.20	0.54
MCS	48.51	44.96	47.15	47.20	0.73

PCS=Physical Component Summary, MCS=Mental Component Summary

Table 6: Comparison of CML patients under treatment for different duration.

SF-36 variables	<=1 years (mean)	1-5 years (mean)	>5 years (mean)	p-value
Physical health				
Physical functioning	81.84	86.00	86.18	0.61
Role physical	73.68	75.00	64.70	0.50
Bodily pain	80.53	84.18	75.60	0.24
General health	59.47	64.83	64.12	0.60
PCS	46.90	49.83	47.77	0.22
Mental Health				
Vitality	63.53	70.16	71.88	0.43
Role Emotions	80.79	77.06	83.31	0.72
Social Functioning	75.00	81.17	78.49	0.59
Mental health	74.84	69.69	73.76	0.50
MCS	47.53	45.28	51.03	0.08

PCS=Physical Component Summary, MCS=Mental Component Summary

Discussions

The principal aim of our study was to compare the QoL outcomes between individuals taking TKIs and control groups. While comparing outcomes of individual components of physical QoL, the outcomes were poor in CML patients taking TKIs, however these findings were not statistically significant. While comparing PCS scores between two groups, PCS score was found to be better in the healthy population compared to CML patients taking TKIs and the difference was significant. (p value 0.01). This

indicates that physical QoL was found to be better among the healthy population compared to CML. Our finding was supported by the study done by Efficace et al. and Phillips et al. which also showed worse physical QoL in CML patients.^{9,14} Poor outcomes in physical QoL of CML patients could be because of the adverse effects of the different TKIs in CML group as mentioned in the various studies. The other reason could be the increased level of therapy related fatigue in CML group limiting the physical QoL as shown by different studies.^{9,14,15}

However, mental QoL was not significantly different between the two groups. MCS was found to be better in CML groups as compared to the healthy population. (MCS of 47.71 in CML group vs 45.12), though these findings were not statistically significant. (p- value 0.09). Vitality (VT) i.e., energy to do work, role emotions (RE) i.e. limitations in work due to emotional problems, social functioning and overall mental health were found to be better in the CML group. (Findings were not significant). The findings aligned to a study by Phillips et al. which also showed no differences in mental QoL between two groups. But the findings differed from study of Efficace et al. which marked impairment in VT and RE in CML patients. (p value of 0.01 and <0.01 respectively).^{14/16} Sex-wise comparison of QoL among the CML patients in this study showed the physical QoL was better in male compared to female and the mental QoL was better in female compared to male. However, these findings were not found to be statistically significant. These findings are in contrary to the findings by Efficace et al., Kyoung et al. and IRIS trial. All these studies noted significant poor QoL in the female CML patients compared to male patients.¹⁶

All age groups of CML patients have similar outcomes when physical QoL was compared. However, statistically significant difference was noted in mental QoL among different age groups. In post hoc analysis, CML patients with 18-39 years' age group i.e., younger patients reported worse QoL compared to other two groups. No difference was seen in QoL among the other groups (40-59 years and >60 years). These findings were consistent to findings of Efficace et al. and Kyoung et al. RE i.e., limitations of work because of emotions and MH were most affected component of mental QoL of 18-39 years' group patient.¹⁶ Some younger patients included in this study were in the process of career development and some others had young family life, thus greater responsibility to the family members which could have caused more mental and emotional stress leading to poor mental QoL in younger CML patients in this study.

The comparison of QoL among CML patients receiving different TKIs did not show any difference in the physical as well as mental QoL. These findings were in contrary to the findings of Adi Shacham et al. and Kyoung et al. Study by Adi Shacham et al. revealed less fatigue, less limitation of daily activities, less body pain, better emotional functioning and less worries in patients with imatinib in comparison to patients with newer generation TKIs (dasatinib and nilotinib), thus better physical and mental QoL in patients with imatinib.¹⁷ Kyoung et al. however noted better QoL outcomes in newer generations TKIs compared to imatinib.¹⁷ While comparing the QoL in CML patients taking TKIs for different durations, there was no difference in physical and mental QoL among patients of

the groups. These findings were dissimilar to the study of Kyoung et al. which reported meaningful worse QoL outcomes in the CML patients taking the TKIs for a longer duration of time.¹⁷

This study had few limitations. It was a cross sectional study design. It is known that the QoL of a person is not only affected by the age and gender of the person. There are a number of factors like economic status, education, geographic area of the person, co morbid condition which could affect the QoL of a person. Since this study compared the QoL between CML and age sex matched a healthy population, other factors could also affect the QoL of a person. Similarly, the control groups included the family members of the admitted patients rather than the general population from the community. This could have also affected the mental QoL of the healthy population. Similarly, the number of patients TKIs other than imatinib was very less. So, QoL comparison between the patients taking different drugs was statistically not meaningful.

Conclusion

The findings of poor physical QoL in CML patients taking TKIs necessitates clinicians to investigate the underlying factors contributing to this decline in QoL.

Since compromised mental QoL was seen among 18-39 years' age group, assessment of psychological impact of the disease and proper counseling is needed for effective improvement in the mental QoL.

It is essential to conduct quality of life (QoL) research on a broader scale among individuals with various chronic conditions, including cancer patients, in Nepal. This research would serve to recognize and effectively tackle the QoL challenges experienced by these patients.

Acknowledgement

I express my profound gratitude to Professor Dr. Gyan Krishna Kayastha and Associate Professor Dr. Nora Ranjitkar from the Department of Internal Medicine, PAHS, for their continuous guidance and support throughout the duration of this study. Additionally, I extend my thanks to the study participants for their willingness to actively participate in this study.

References

- Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J. Harrison's Principles of Internal Medicine. Vol I. 20th ed. Mc Graw-Hill Education; 2018.
- Hoffmann VS, Bacarani M, Hasford J, et al. The EUTOS population-based registry: Incidence and clinical characteristics of 2904 CML patients in 20 European Countries. *Leukemia*. 2015;29(6):1336-1343. DOI: [10.1038/leu.2015.73](https://doi.org/10.1038/leu.2015.73) PMID: 25783795
- Thompson PA, Kantarjian HM, Cortes JE. Diagnosis and Treatment of Chronic Myeloid Leukemia in 2015. *Mayo Clin Proc*. 2015;90(10):1440-1454. DOI: [10.1016/j.mayocp.2015.08.010](https://doi.org/10.1016/j.mayocp.2015.08.010) PMID: 26434969 PMCID: PMC5656269
- Cella D, Nowinski CJ, Frankfurt O. The impact of symptom burden on patient quality of life in chronic myeloid leukemia. *Oncol*. 2014;87(3):133-147. DOI: [10.1159/000362816](https://doi.org/10.1159/000362816) PMID: 25012261
- Jabbour E, Kantarjian H. Chronic myeloid leukemia: 2018 update on diagnosis, therapy and monitoring. *Am J Hematol*. 2018;93(3):442-459. DOI: [10.1002/ajh.25011](https://doi.org/10.1002/ajh.25011) PMID: 29411417
- Sawyers Charles L. CHRONIC MYELOID LEUKEMIA. Published online 1999. DOI: [10.1056/NEJM199904293401706](https://doi.org/10.1056/NEJM199904293401706) PMID:10219069
- Unnikrishnan R, Veeraiah S, Ganesan P. Symptom burden and quality of life issues among patients of chronic myeloid leukemia on long-term imatinib therapy. *Indian J Med Paediatr Oncol*. 2017;38(2):165-168.
- Efficace F, Cannella L. The Value of Quality of Life Assessment in Chronic Myeloid Leukemia Patients Receiving Tyrosine Kinase Inhibitors. www.haematologica.org
- Efficace F, Bacarani M, Breccia M, et al. Chronic fatigue is the most important factor limiting health-related quality of life of chronic myeloid leukemia patients treated with imatinib. *Leukemia*. 2013;27(7):1511-1519. DOI: [10.1038/leu.2013.51](https://doi.org/10.1038/leu.2013.51) PMID: 23417029
- Kayastha GK, Gurung P, Acharya PK, et al. Patan hospital experience in treating philadelphia chromosome/BCR-ABL1 positive chronic myeloid leukemia patients with gleevec (imatinib mesylate); the first generation specific tyrosine kinase inhibitor. *BMC Blood Disord*. 2010;10. DOI: [10.1186/1471-2326-10-8](https://doi.org/10.1186/1471-2326-10-8) PMID: 21138592 PMCID: PMC3017013
- Kayastha GK, Ranjitkar N, Gurung R, et al. Treating Philadelphia chromosome/BCR-ABL1 positive patients with Glivec (Imatinib mesylate): 10 years' experience at Patan Hospital, Nepal. *Br J Haematol*. 2017;177(6):991-999. DOI: [10.1111/bjh.14645](https://doi.org/10.1111/bjh.14645) PMID: 28369812
- Ware JE, Ware J. SF-36 Physical and Mental Health Summary Scales: A User's Manual Estimation of Medical Care Total Expenditures View Project.; 1993.
- Koirala BP, Pandey RA, Dhungana GP, Twi JT, Byanju S, Khawas B. Quality of Life of Patients Undergoing Cancer Treatment in. *Am J Cancer Prev*. 2015;3(2):35-44. doi:10.12691/ajcp-3-2-3
- Phillips KM, Pinilla-Ibarz J, Sotomayor E, et al. Quality of life outcomes in patients with chronic myeloid leukemia treated with tyrosine kinase inhibitors: A controlled comparison. *Support Care Cancer*. 2013;21(4):1097-1103. DOI: [10.1007/s00520-012-1630-5](https://doi.org/10.1007/s00520-012-1630-5) PMID: 23179489
- Poort H, Meade CD, Knoop H, Gielissen MFM, Pinilla-Ibarz J, Jacobsen PB. Adapting an Evidence-Based Intervention to Address Targeted Therapy-Related Fatigue in Chronic Myeloid Leukemia Patients. *Cancer Nurs*. 2018;41(1):E28-E37. DOI: [10.1097/NCC.0000000000000446](https://doi.org/10.1097/NCC.0000000000000446) PMID: 27832018 PMCID: PMC5422141
- Efficace F, Bacarani M, Breccia M, et al. Health-related quality of life in chronic myeloid leukemia patients receiving long-term therapy with imatinib compared with the general population. *Blood*. 2011;118(17):4554-4560. DOI: [10.1182/blood-2011-04-347575](https://doi.org/10.1182/blood-2011-04-347575) PMID: 21750313
- Kim KH, Kim DY, Kim SH, et al. Survey of QoL (quality of life) on Patients Receiving Tyrosine Kinase Inhibitors for Chronic Myeloid Leukemia: Korean CML Working Party Group. *Blood*. 2015;126(23):5166-5166. DOI: [10.1182/blood.V126.23.5166.5166](https://doi.org/10.1182/blood.V126.23.5166.5166)
- Shacham A, Rosenmann L, Leader A, Sharf G, Raanani P, Rozovski U. Patient Reported Outcomes (PROS) show Superior Quality of life (QOL) for Chronic Myeloid Leukemia (CML) patients treated with first compared to newer generations of Tyrosine Kinase Inhibitors (TKIS). *J*. 2019;3:1. DOI: [10.1097/01.HS9.0000566260.60138.6d](https://doi.org/10.1097/01.HS9.0000566260.60138.6d)