Original Research Article

DEMOGRAPHICS AND OVERALL SURVIVAL PATTERN OF CHRONIC MYELOID LEUKEMIA IN A TERTIARY HOSPITAL IN SOUTH-SOUTH NIGERIA: THE CALABAR EXPERIENCE

Abstract

Background: CML is a bi- or triphasic disease comprising of the chronicphase (present at diagnosis in approximately 85% of patients) which can easily be controlled with conventional chemotherapy, followedby unstable accelerated phase and terminating in ablastic phase. The treatment of CML has evolved over the years The availability of the tyrosine kinase inhibitors has distinctly changed the disease course for patients with Ph+ and/or BCR-ABL1+ (CML).This study aims to determine the demographics and overall survival patterns of CML patients in the University of Calabar Teaching Hospita(UCTH)l**Method:**The study is a retrospective study of CML patients seen and managed at the UCTHfrom June 2014 to August 2021. Male/female distribution was 9/13, with a median age of 42 years. Overall survival (OS) and progressionfree survival (PFS) were determined using the Kaplan-Meier techniques. The data were analyzed using Microsoft Excel 2016 and IBM SPSS version 21. **Result:** Total of 22 CML patients were seen over the 8-year-period of review. The mean age was 42.63, median age 42, and modal age was 37 years respectively. There were 9 males and 13 females. 20 of the patients were in the chronic phase while 2 were in the terminating blastic phase. The presence of mutation was seen in two patients while the remaining 20 showed no mutation. Of the patients, 6 were dead and 16 are alive at the time of review. The overall survival period ranges from 12 to 84 months. The survival distributions for mutation and state of the disease (chronic or blastic) were not statistically significantly different, $X^2 = 3.204$, $p = 0.073$.**Conclusion**There is inconsistency in the demographic and overall survival pattern of chronic myeloid leukaemia in our environment with providing factors that can mitigate financial constrain,policyformulation,ease of diagnosis and accessibility of TKI

Keywords: CML, Survival pattern, Calabar

Introduction

Chronic myeloid leukaemia (CML) is a clonal myeloproliferative disorder characterized by the presence of a complete spectrum of myeloid development in the peripheral blood. This is caused by the BCR-ABLI, a chimeric protein which is the result of the reciprocal translocation [t (9, 22) (q34: q11)] which is cytogenetically represented as Philadelphia chromosome (ph) [1,2]. CML is a rare disease condition, with an incidence of one to two cases per 100,000 people per year and accounts for 15% of adult leukaemia and 15.97% of leukaemia globally [3].CML is said to affect any age group but is rare in children [2,3]. The median ages vary from one location to another. In the western world, it is 53 years while in African countries, it is 38years [5, 6, 7]. CML is a bi- or tri-phasic disease condition. However, these disease phases are associated with increased mortality, not until the discovery of tyrosine kinase inhibitors which has improved the management and overall survival of CML patients. There is variation in the demographic and overall survival pattern of CML, Smith et al [9] reported in the United Kingdom 5-year relative survival estimates for men and women diagnosed in 2004–2011 and treated with TKIs over the period 2004–2013 were 89.1% (79.9% to 95.4%) and 90.1% (71.9% to 96.1%), respectively.Druker et al also reported a similar value of 5years of survival in the UK [10]. However, another study conducted in Nigeria by Oyekunle et al reported a lower value of 63% overall survival of CML in the chronic phase at 5 years [11]. Thus, this is inferior to most studies in western countries. Furthermore,Hochhaus et al. [13] reported a 6-year OS of 76% among a cohort of 532 late CP-CML patients, managed on imatinib after interferon. Similarly, Kantarjian et al. [14] reported 8-year survival of 87%, among those patients managed during the imatinib era. This study aims to determine the demographics and overall survival patterns of CML patients in the University of Calabar Teaching Hospital.

Materials and Methods:

Study Design: This study was a retrospective study of chronic myeloid leukaemia patients seen at the University of Calabar Teaching Hospital seen from June 2014 to August 2021

Study Area: The hospital is a 600-bed tertiary health institution that renders specialist care to its host and neighbouring communities.

Subject: This included patients diagnosed with chronic myeloid leukaemia at our facilities who had commenced any form of tyrosine kinase inhibitor and are also compliant with hospital visits at the haematology department, which is staffed by consultants, resident doctors, trained nurses and laboratory scientific officers. The diagnosis was made by the haematologist using peripheral blood and bone marrow. In addition, the further investigation included cytogenetics and karyotyping majorly, BCR-ABRL and Philadelphia (ph) respectively.

Selection Criteria: Those whose information was retrieved from the cancer registry, hospital records and patients' folders were included in the study, while omissions and discrepancies from any part of the archives were excluded from the study.

These data and results collated were analyzed using Microsoft Excel 2016 and IBM SPSS version 21. The data were analyzed using Simple Inferential Statistics (frequency and

percentage) Survival analysis was done using the Kaplan-Meier method. For the survival studies, overall survival (OS) was calculated as the time interval between the time of diagnosis to the date of last follow-up (for living patients) or the date of death from any cause.Please state the significance level

Results: Total of 22 CML patients were seen over the 8-year-period of review. The demographic characteristics of the patients are presented in table 1. The mean age was 42.63, median age 42, and modal age was 37 years respectively. There were 9 males and 13 females. 20 of the patients were in the chronic phase while 2 were in the terminating blastic phase. The presence of mutation was seen in two patients while the remaining 20 showed no mutation. Of the patients, 6 were dead and 16 are alive at the time of review. The overall survival period ranges from 12 to 84 months. Figure 1 showed the year of diagnosis and the Kaplan Meier curve for the state of disease and presence or absence of disease are presented in figures 2 & 3 respectively.

1. **Each Table and Figure should be interpreted separately since they carry different information. 2. Also the interpretation should come before the Table or Figure. 3. The Result and Table or Figure should be caption with the same tittle for better understanding.**

Table 1: Showing the Demographic Characteristics of the participants

VARIABLE	FREQUENCY (n=22)	PERCENTAGE
Age Range		
20-29	3	13.64
30-39	6	27.27
40-49	7	31.82
50-59	4	18.18
≥60	2	9.09
Gender		
Male	9	40.91
Female	13	59.09
State of disease		
Chronic	20	90.91
Blastic	2	9.09
Mutation		
Present	2	9.09
Absent	20	90.91
Status		
Dead	6	27.27
Alive	16	72.73
Overall Survival (Months)		
12	7	31.82
24	5	22.73
36	1	4.55
48	2	9.09
60	4	18.18
84	3	13.64

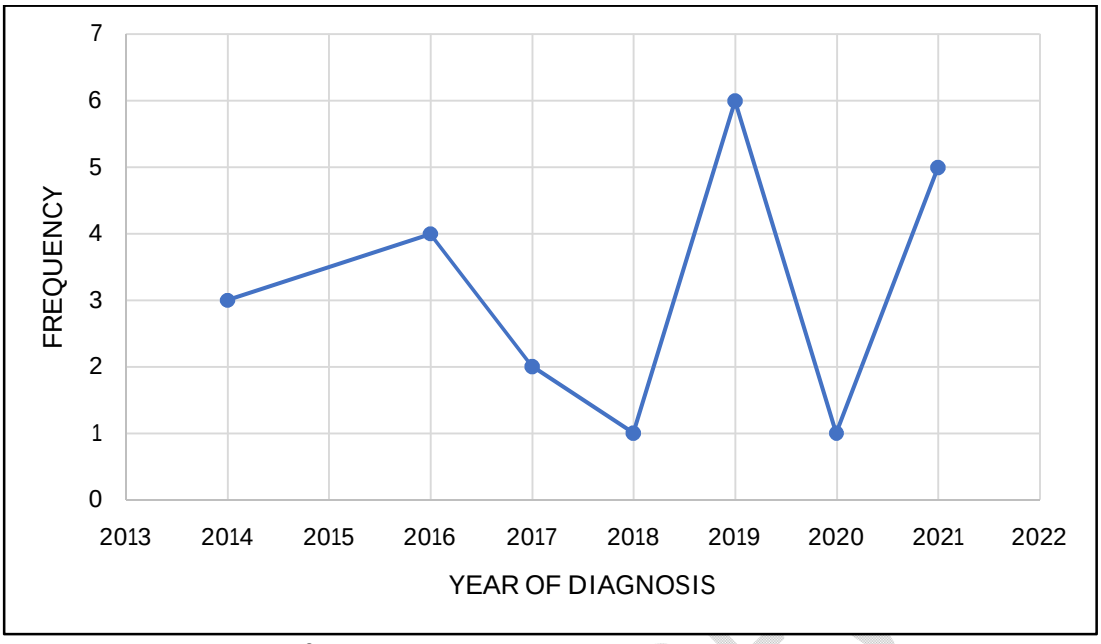

Figure 1: Showing the year of disease diagnosis

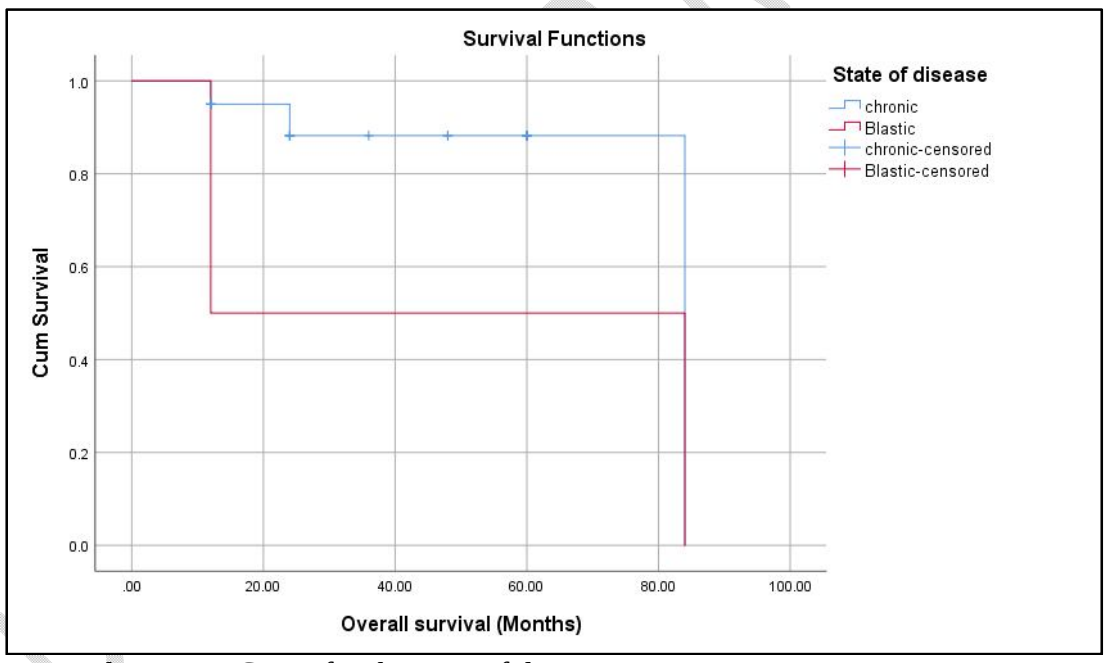

Figure 2: Kaplan Meier Curve for the state of disease

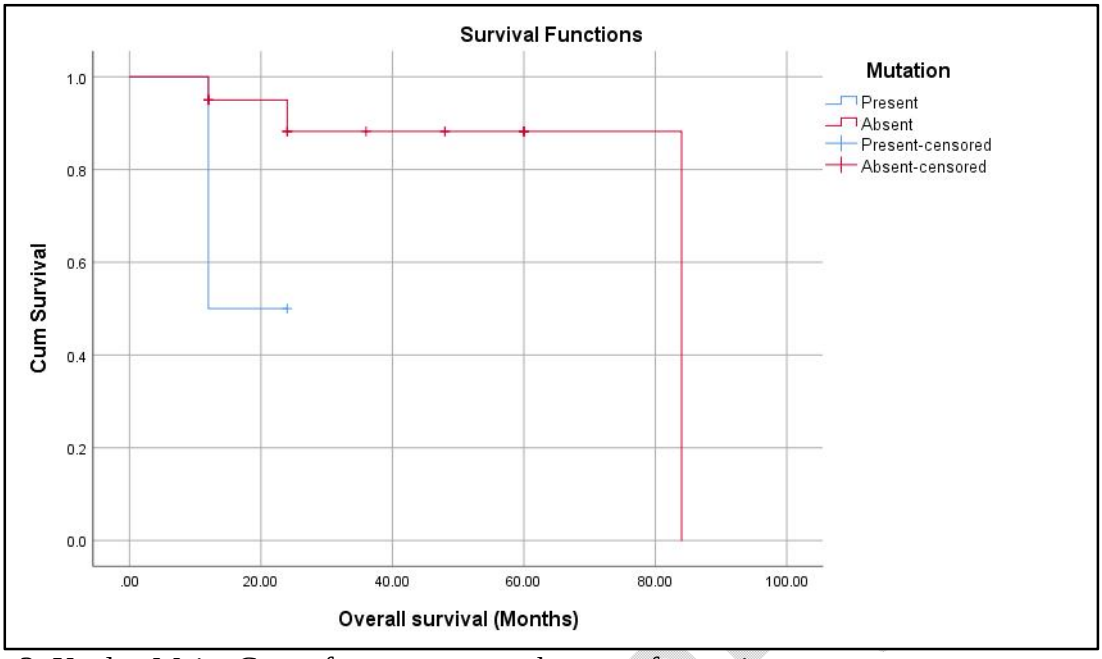

Figure 3: Kaplan Meier Curve for presence or absence of mutation

A Breslow (Generalized Wilcoxon) test was run to determine the differences in the survival distribution of the patients diagnosed with chronic myeloid leukaemia. The survival distributions for mutation and state of the disease (chronic or blastic) were not statistically significantly different, $X^2 = 3.204$, $p = 0.073$.

DISCUSSION

This study shows inconsistency with the available data on chronic myeloid leukaemiaconcerning age, sex and overall survival. Chronic myeloid leukaemia constitutes 2percent of all the malignancies seen during the period review. This study also reported female preponderance with an M:F ratio of 1:1.5. this is similar to a previous study by Akaba et al [4].This difference can be attributed to the early health-seeking behaviour among women compared to men.

The median age of chronic myeloid leukaemia patients in this study was 45 years, which is similar to the study by Koffi et al on positive chronic–phase myeloid leukaemia in Ivory Coast [14]. Furthermore, this finding is also somewhat similar to the finding of Oyekunle et al [15] on the overall survival pattern of CML, but at variance with the study conducted by Hoglund et al [16] that reported a higher value. This difference in age incidence of CML can be attributed to a combination of environment and as yet unknown biological factors that may account for the differential age incidence pattern of CML between the Blacks and the other races[17]. This study also shows that 90.91% and 9.09% were in chronic and blastic phasesrespectively, this is similar to the study by Durosinmi et al on the use of Imatinibmesylate in Nigeria with CML [17]. This study also reviews that 9.09% had the mutation and six[6]death respectively.

This study also reported a median overall survival of 24 months with 5 patients. Overall survival at 12, 24, 36, 48, 60, 84 months was 31.82%, 22.73%, 4.55%, 9.09%, 18.18% and 13.64% respectively. This study is at variance with a similar study conducted by Oyekunle et al at ObafemiAwolowo University Teaching Hospital (OAUTH),Ile-Ife,South-West Nigeria. This

difference in overall survival rate can be attributed to OAUTH as the only centre where tyrosine kinase inhibitors can be accessed in the country.The cost and psychological implication to the patient from other regions of the country are quite unbearable and challenging predisposing to non-adherence, transformation, loss to follow up and eventually death.

CONCLUSION;There is inconsistency in the demographic and overall survival pattern of chronic myeloid leukaemia in our environment with providing factors that can mitigate financial constrain,policyformulation,ease of diagnosis and accessibility of TKI

REFERENCES

1. Sawyers C. Chronic myeloid leukemia. *N Engl J Med.* 1999;340:1330–1340.

2. Druker BJ, Sawyers CL, Kantarjian H, et al. Activity of a specific inhibitor of the BCR-ABL tyrosine kinase in the blast crisis of chronic myeloid leukemia and acute lymphoblastic leukemia with the Philadelphia chromosome. *N Engl J Med.* 2001;344(14):1038–1042.

3. Akaba K, Enang O, Igwilo H, Eduve V, Akaba E, Cletus O, Oshatuyi O. Demographic pattern of chronic lymphocytic leukemia in a tertiary hospital in Calabar, South-South Nigeria. Ann Afr Med. 2020 Jul-Sep;19(3):203-206. doi: 10.4103/aam.aam_60_19. PMID: 32820734; PMCID: PMC7694702.

4. K. Akaba, P. Osho, O. Oshatuyi, E. Akaba and V. Eduve. A profile of leukaemias in adults managed at the university of calabar teaching hospital in Nigeria. East African Medical Journal Vol. 96 No. 3 March 2019.

5. Thygesen LC, Nielsen OJ, Johansen C. Trends in adult leukemia incidence and survival in Denmark, 1943-2003. *Cancer Causes Control.* 2009;20:1671–80.

6. Smith A, Howell D, Patmore R, Jack A, Roman E. Incidence of haematological malignancy by sub-type: A report from the Haematological Malignancy Research Network. *Br J Cancer.* 2011;105:1684–92.

7. Tomeczkowski J, Leisten MK, Metin H, Khuen C, Fleischmann J, Tapprich C. Prevalence and Treatment of Chronic Lymphocytic Leukaemia (Cll) In Germany: An .Analysis of Sickness Funds. *Value Health.* 2014;17:A524.

8. Akaba K, Nwogoh B, Akpan I, Bassey OB, Effiong O, Petters E, et al. Epidemiological pattern of adult haematological malignancies in a tertiary hospital in cross river state. *Int Res J Oncol.* 2019;2:1–9.

9. Smith AG, Painter D, Howell DA, Evans P, Smith G, Patmore R, Jack A, Roman E. Determinants of survival in patients with chronic myeloid leukaemia treated in the new era of oral therapy: findings from a UK population-based patient cohort. BMJ Open. 2014 Jan

15;4(1):e004266. doi: 10.1136/bmjopen-2013-004266. PMID: 24435897; PMCID: PMC3902525.

10. Gupta N, Mahapatra M, Seth T, Tyagi S, Sazawal S, Saxena R. Social and Financial Barriers to Optimum TKI Treatment in Patients with Chronic Myeloid Leukemia-A Knowledge-Attitudes-Practices Study from India. Mediterr J Hematol Infect Dis. 2021 Jan 1;13(1):e2021004. doi: 10.4084/MJHID.2021.004. PMID: 33489043; PMCID: PMC7813279.

11. Oyekunle AA, Durosinmi MA, Bolarinwa RA, Owojuyigbe T, Salawu L, Akinola NO. Chronic Myeloid Leukemia in Nigerian Patients: Anemia is an Independent Predictor of Overall Survival. Clin Med Insights Blood Disord. 2016 Jun 20;9:9-13. doi: 10.4137/CMBD.S31562. PMID: 27375361; PMCID: PMC4915783.

12. Hochhaus A, Druker B, Sawyers C, Guilhot F, Schiffer CA, Cortes J, Niederwieser DW, Gambacorti-Passerini C, Stone RM, Goldman J, Fischer T, O'Brien SG, Reiffers JJ, Mone M, Krahnke T, Talpaz M, Kantarjian HM. Favorable long-term follow-up results over 6 years for response, survival, and safety with imatinibmesylate therapy in chronic-phase chronic myeloid leukemia after failure of interferon-alpha treatment. Blood. 2008 Feb 1;111(3):1039-43. doi: 10.1182/blood-2007-07-103523. Epub 2007 Oct 11. Erratum in: Blood. 2008 Jul 15;112(2):452. Gambacorti, Carlo [corrected to Gambacorti-Passerini, Carlo]. PMID: 17932248.

13. HagopKantarjian, Susan O'Brien,Elias J,Guillermo G,Alfonso Q,Jenny S,Mary B. R,Farhad R,Stefan F,Tapan K, Gautam B, Xuelin H, Richard C, Moshe T, Jorge C.Improved survival in chronic myeloid leukemia since the introduction of imatinib therapy: a single-institution historical experience. *Blood* (2012) 119 (9): 1981–1987.

14. Koffi, K.G., Nanho, D.C., N'dathz, E., Kouehion, P., Dissieka, R., Attia, A., et al. (2010) The Effect of ImatinibMesylate for Newly Diagnosed Philadelphia Chromosome-Positive, Chronic-Phase Myeloid Leukemia in Sub-Saharan African Patients: The Experience of Côte d'Ivoire. Advances in Hematology, 2010, Article ID: 268921. https://doi.org/10.1155/2010/268921

15 Anthony A. Oyekunle, Rahman A. Bolarinwa, Adesola T. Oyelese, LateefSalawu, Muheez A. Durosinmi, "Determinants of Overall and Progression-Free Survival of Nigerian Patients with Philadelphia-Positive Chronic Myeloid Leukemia", Advances in Hematology, vol. 2015, ArticleID 908708, 5 pages, 2015. https://doi.org/10.1155/2015/908708.

16. Hoglund M, Sandin F, Hellstrom K, Bjoreman M, Bjorkholm M, Brune M, et al. Tyrosine kinase inhibitor usage, treatment outcome, and prognostic scores in CML: report from the population-based Swedish CML registry. Blood. 2013;122(7):1284–92.

17. Prof. Muheez A. Durosinmi, Prof. Julius O. Faluyi, Dr. Anthony A. Oyekunle, Dr. LateefSalawu, Dr. Ismail A. Adediran, Dr. Norah O. Akinola, et al. The use of Imatinibmesylate in Nigerians with chronic myeloid leukemia.Volume 1, Number 2, doi 10.3205/ctt-2008-en-000027.01.