Journal of Cancer Biomoleculars and Therapeutics

ETERNO PRESS

Article

Clinical Presentation of Chronic Myeloid Leukaemia and Its Correlation with Haematological Parameters in Kenya

Nicholas Anthony Othieno-Abinya[1,*], Joseph David M Maina[1], Angela Awino McLigeyo[2], Andrew Oluoch Odhiambo[3], Sitna Ali Mwanzi[4], Peter Omondi Oyiro[3], Matilda Ong'ondi[4], Shadrack Bonginkosi Shoba[3], Mohammed Ezzi[3], Robert Yatich Bett[3], Maureen Mukanga[5], Kevin Owuor[6], Pier Paolo Piccaluga[7,8,*]

[1]Nairobi Hospital Cancer Centre. P.O. Box 2621 - 00202 Nairobi, Kenya

[2]Kenyatta University, Department of Internal Medicine and Therapeutics, P.O Box 43844-00100 Nairobi, Kenya

[3]The University of Nairobi, Department of Clinical Medicine and Therapeutics, P.O Box 19676-00202 Nairobi, Kenya

[4]Cancer Treatment Centre, Department of Hematology/Oncology Kenyatta National Hospital, Nairobi, Kenya

[5]Novartis Global Health, NVS Kenya Limited, Nairobi, Kenya

[6]Centre for Global Health Research, Kenya Medical Research Institute, Kisumu, Kenya, School of Biological Sciences, University of Nairobi, Nairobi, Kenya

[7]Biobank of Research, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy

[8]Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna, Italy

[*]Corresponding author: Nicholas Anthony Othieno-Abinya, naoabinya@gmail.com; Pier Paolo Piccaluga, pierpaolo.piccaluga@unibo.it

Article history

Received: 27 March 2025
Revised: 23 May 2025
Accepted: 2 July 2025
Published online: 2 July 2025

Keywords

Chronic myeloid leukaemia
Presenting symptoms
Clinical findings
BCR:ABL1
Blood counts
Bone marrow blasts

Abstract

Background: Chronic myeloid leukaemia (CML) is commonly asymptomatic and is discovered incidentally in up to about 50% of patients in chronic phase, due to abnormally high white blood cell (WBC) counts. Commonest symptoms include fatigue and abdominal pain/discomfort, while some patients present with bleeding tendencies. Unusual manifestations include hearing and visual loss.

Methods: This was a retrospective analysis of data from patients attending the Glivec International Patient Assistance Clinic at the Nairobi Hospital between January 2006 and December 2018. In-formation sourced included demographic profiles, findings on physical examination, and laboratory values. Absolute, range, median and mean counts for white blood cells (WBC $\times 10^9$/l), ab-solute neutrophil count (ANC$\times 10^9$/l), platelets (PLT $\times 10^9$/l), haemoglobin (hgb, g/dl), *BCR:ABL1* baseline levels, and bone marrow blast percentage at diagnosis. All parameters were tested against each of the clinical presentations.

Results: We enrolled 583 patients; the mean age was 39.8 years. The commonest symptom was abdominal swelling in 235 cases (40.3%); 70 (12%) experienced abdominal pain. Priapism occurred in 4 males (0.69%), blindness and deafness in 8 patients (1.37%). Splenomegaly was significantly more common among males than females (P = 0.015). Patients aged ≤ 20 years were more likely to be in heart failure (P = 0.032); leg swelling was more in those with high platelet counts (p=0.023). Unclear presentations were more common in those with high WBC counts (p=0.015). Total WBC counts and *BCR:ABL1* levels were higher among younger patients (p=0.036, and 0.025, respectively). Patients with leg swelling had lower *BCR:ABL1* levels (p=0.005), those in heart failure had significantly higher *BCR:ABL1* levels at baseline compared with the rest (p=0.037). Patients with lymphadenopathy were more likely to have lower ANCs (p=0.035). Patients who had pallor had a significantly lower *BCR:ABL1* values compared with those without (P = 0.025). Similarly, patients who had leg swelling had a significantly lower mean BCR:ABL1 percentage compared with those without (P = 0.005). In contrast, those in heart failure had significantly higher mean *BCR:ABL1* values (P = 0.037). Those with lymphadenopathy had significantly lower absolute neutrophil counts compared with those without (P =0.035).

Conclusions: Clinical manifestations of CML cannot be explained merely by haematologic values. Complex biologic and physico-chemical factors should be further interrogated.

1. Introduction

Chronic myeloid leukaemia (CML) commonly presents insidiously, and in up to 50% of the patients the disease is identified incidentally in the chronic phase because of abnormally elevated white cell counts or enlarged spleen [1]. Splenomegaly rates at presentation vary between series, from 46%-76%.2,3 There are also nonspecific symptoms such as fatigue, weight loss, decreased energy, or decreased exercise tolerance [2]. These latter manifest after the disease has occurred for a long time. The splenic enlargement is explained by an increase in the number of white cells in circulation, whereas fatigue and exercise intolerance are explained on anaemia [3,4]. Bleeding can be observed, related to platelet dysfunction rather than thrombocytopenia, which occurs in advanced phases. There are also rare presentations such as hearing loss, visual loss, and priapism. The latter are taken to be manifestations of hyperviscosity, resulting from high WBC counts more than 250×10^9/litre [5,6].

In a preliminary report of this study, patients with impaired vision and/or hearing, or CNS manifestations had significantly higher mean total WBC counts ($p = 0.03$) [7]. Overall, no study has looked systematically at the correlation between clinical manifestations of CML and values of various haematopoieic elements, least so baseline *BCR:ABL1/ABL1* percentage and baseline bone marrow blast percentage.

The objective of this study was explore the relationship between clinical symptoms and signs with haematologic parameters including baseline *BCR:ABL1/ABL1* levels.

2. Materials and Methods

2.1 Case Series

Five hundred thirty-eight patients treated at the Nairobi Hospital Glivec International Patient Assistance Program (GIPAP) Clinic between January 2006 and December 2018 inclusive were studied. All patients for which clinical records were available were included, without any further selection. We retrospectively analyzed demographic data, the initial presenting complaints and physical examination findings at the time of first contact at the clinic. We also analyzed laboratory values that were taken at the time of initial presentation. Absolute, range, median and mean counts for white blood cells (WBC $\times10^9$/l), neutrophils (ANC$\times10^9$/l), platelets (PLT $\times10^9$/l), haemoglobin (hgb, g/dl), bone marrow blast percentage, and entry *BCR:ABL1* values, were analyzed against each of the clinical presentations.

2.2 Statistical Analysis

Fisher's exact test was used to analyze contingency tables, Chi-square test was used to test observed values against the expected values, Pearson Chi2 test to test categorical data, Rank sum test (Mann-Whitney U test) to test nonparametric null hypothesis, Kruskal–Wallis test to compare values from different sample sizes, and t-test to determine differences between means of two groups. In the whole cohort, data distribution is assumed to be normal. However, non-parametric tests were used for sub-analysis based on smaller sample sizes.

3. Results

We enrolled a total of 583 patient, including 322 males (55.2%) and 261 females (44.8), with a male:female ratio of 1.2:1. Mean age was 39.7 years, with 265 patients (45.6%) being in the age range 21-40 years. Symptoms and laboratory values were available in all cases. Clinical signs were consistently assessed and available for analyses in 107 patients.

3.1. Symptoms at Presentation

Twenty-five females (9.6%) and 45 males (14%) presented with abdominal pain. Abdominal swelling was a presentation among 103 females (39.5%) and 132 males (41%). Dizziness, fever and malaise presented in 67 females (25.7%) and 104 males (32.3%). Swelling of legs was a presentation among 11 females (4.2%) and 25 males (7.8%). Priapism occurred in 4 males (0.69%), blindness and deafness in 8 patients (1.37%). Thirty-three females (12.6%) and 35 males (10.9%) presented with miscellaneous other symptoms, (Table 1 and Supplementary Table 1)

Table 1. Patients' demographic characteristics

Demographics	***Values***
Sex n (%) [n= 583]	
Female	261 (44.8)
Male	322 (55.2)
Age (Years) Mean [SD]	39.7 (15.04)
Age category (Years) n (%) [n=581*]	
1-20	51 (8.8)
21-40	265 (45.6)
41-60	208 (35.8)
61+	57 (9.8)

* For two patients the date of birth in the files were not consistent and were therefore excluded.

3.2 Baseline Clinical Signs by Gender

Females evaluable were 41 and males 66. Pallor was documented in 21 females (51.2%) and 30 males (45.5%). Splenomegaly was recorded in 30 females (73.2%) and 60 males (90.9%), the difference being statistically significant ($p=0.015$). Wasting was found in 4 females (9.8%) and 9 males (13.6%). Leg swelling was found in 3 females (7.3%) and 11 males (16.7%). Heart failure was registered in 3 females (7.3%) and 7 males (10.6%). Lymphadenopathy was detected in 3 females (7.3%) and 5 males (7.6%). Other signs were recorded in 14 females (34.1%) and 25 males (37.9%).

3.3 Baseline Clinical Signs by Age (n=107)

Six out of 13 patients aged ≤20 (46.2%), 23 aged 21-40 (49%), 50 aged 41-60 (6.50%) and 4 of 11 aged ≥61 (36.4%) were recorded as pale. Splenomegaly was recorded in 11 of 13 patients aged ≤20 years (84.6%), 42 of 47 aged 21-40 (89%), 29 of 36 aged 41-60 (80.6%), 8 of 11 aged ≥ 61 (72.7%). Wasting was recorded in 2 of 13 aged ≤20 (15.4%), 8 of 47 aged 20 – 40 (17%), 3 of

36 aged 41 – 60 (8.3%) and 0 of 11 aged ≥61 (0%). Leg swelling was recorded in 3 of 13 aged ≤20 years (23.1%), 5 of 47 aged 21-40 (11%), 4 of 36 aged 41-60 (11.1%) and 2 of 11 aged ≥60 (18.2%).

Four of 13 patients age ≤20 (30.8%) were diagnosed with features of heart failure, which was also documented in 4 out of 47 aged 21-40 (8.5%), 2 of 36 aged 41-60 (5.6%) and none of 11 aged ≥60 (0%). Patients in the younger age group (≤20) were more likely than older patients to present in heart failure (Pearson chisquare = 8.8255; Pr = 0.032], the difference being statistically significant.

Lymphadenopathy was recorded in 2 of 13 patients aged ≤20 years (15.4%), 5 of 47 aged 21-40 (11%), 1 of 36 aged 41-60 (2.8%), 0 of 11 aged ≥ 61 (0%), and the differences were not significant. Other miscellaneous findings were documented in 8 of 13 aged ≤20 (61.5%, 17 of 47 aged 21-40 (36%), 10 of 36 aged 41-60 (27.8%) and 4 of 11 aged ≥61 (36.4%).

Lowest age group (≤ 20 years) also had a significantly higher median initial total WBC counts than other age groups (p =0.036). The same age group had significantly higher median *BCR:ABL1* values compared with the other age groups (p=0.025) (Figure 1).

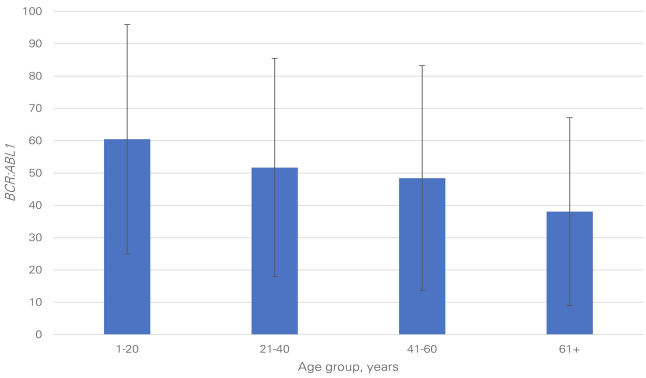

Figure 1. *BCR:ABL1* levels, as measured by quantitative RT-PCR (y-axys) in different age groups (x-axys). Transcript copies at diagnoses are plotted. Significant differences were recorded by ANOVA (p=0.0124) and Kruskal-Wallis (p=0.025).

3.4 Baseline Clinical Signs in Relation to Laboratory Values

The median interquartile ranges (IQR) were computed and compared.

3.4.1 Pallor (n=107)

Median IQR of total white blood cell counts was 267 for those who were pale and 223 for those who were not (p=0.301). For initial platelet count for those who were pale it was 288 and 336 for those who were not (p=0.135). The value for original haemoglobin was 8.7 for those who were pale and 9 for those who were not (p=0.446).

For initial absolute neutrophil count for those who were pale it was 152 and 127 for those who were not (p=0.727). For initial bone marrow blasts for those who were pale it was 4 and also 4 for those who were not pale (p=0.745).

Mean BCR:ABL1 for those who were pale was 47.6% and 63.8% for those who were not pale (p=0.025), statistically significant.

3.4.2 Splenomegaly (n=107)

The median interquartile ranges (IQR) of various baseline laboratory values in relation to splenomegaly are given based on rank sum test (Supplementary Table 1). Baseline total white blood cell counts for those who had splenomegaly was 280.5 × 10^9/litre and 188.5 × 10^9/litre for those who did not (p=0.17). Absolute neutrophil counts were 136.5 × 10^9/litre against 113.7 × 10^9/litre (p=0.951), platelet counts were 301.7 × 10^9/litre against 298.5 × 10^9/litre (p=0.548), haemoglobin levels were 8.6g/dl against 9.2g/dl (p=0.164), bone marrow blast counts were 4% against 4% (p=0.548), *BCR:ABL1* levels were 55.2% against 63.5% (p=0.383).

None of the laboratory value tested correlated significantly with splenomegaly.

3.4.3 Wasting (n=107)

The median IQR of initial total WBC count for those who were wasted was 267 and 260 for those who were not (p=0.935). For initial PLTs counts for those who were wasted it was 336 and 290 for those who were not (p=0.242).The value for initial haemoglobin for those who were wasted was 8.9 and 8.7 for those who were not (p=0.859). Initial absolute neutrophil counts for those who were wasted had a value of 163 × 10^9/L and 128 × 10^9/L for those who were not (p=0.183).The median IQR of bone marrow blasts for those who were wasted was 5.5 and 4 for those who were not (p=0.42).The value of BCR:ABL1 for those who were wasted was 39% and 56 for those who were not (p=0.37).

3.4.4 Leg swelling (n=107)

Leg swelling was defined as increase in legs/thighs diameter, without clinical evidence of oedema (Figure 2). In a few instances, the painless subcutaneous tissue was punctured and unclotted bloody fluid was collected. This finding, to the best of our knowledge, was never described before.

Median IQRs for leg swelling were as follows: for initial total WBC count for those who had leg swelling it was 308 and 254 for those who did not have (p = 0.55). For initial platelet counts for those who had leg swelling it was 310.5 and 291 for those who did not (P = 0.819). For initial haemoglobin for those who had leg swelling it was 8.7 and 8.8 for those who did not (p = 0.523). For initial absolute neutrophil count for those who had leg swelling it was 165 and 127.5 for those who did not (p = 0.328). For bone marrow blasts the value was 4.5 for those who had leg swelling and 4 for those who did not (p = 0.328). The initial *BCR:ABL/ABL* for those who had leg swelling was 31% and 60.5% for those who did not [t – test (97df) = 2.86, (p = 0.005)], the difference being statistically significant.

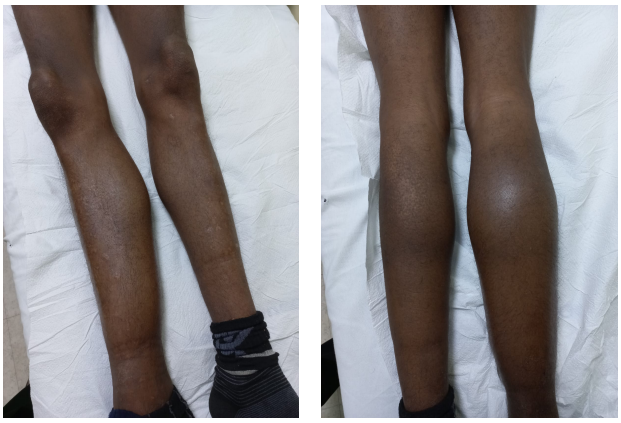

Figure 2. Leg swelling in CML patients due to subcutaneous blood deposition (A, posterior view; B, antero-lateral view). The image illustrates the characteristic tissue swelling where blood accumulates in the subcutaneous tissue. This deposition results from increased vascular permeability and impaired lymphatic drainage, leading to noticeable massess. The affected area shows a marked increase in volume, with the skin appearing taut and sometimes displaying a reddish or purplish discoloration due to extravasated blood cells.

3.4.5 Heart Failure (n=107)

Median IQR of initial total WBC count for those who had heart failure was 378.5 and that for those who did not was 247 (P = 0.145). The initial platelet count for those who had HF was 234 and 313 for those who did not (P = 0.113). The initial haemoglobin level at presentation for those who had heart failure was 8.1 and for those who did not it was 8.8 (p = 0.661). The median initial absolute neutrophil count for those who had heart failure was 135 and 132.5 (P = 0.701).The median initial platelet counts for those in heart failure was 234 and that for those who did not was 313 (P = 113). The median initial bone marrow blasts for those in heart failure was 5.5 and that for those who were not was 3.5 (P = 0.733). The median initial *BCR:ABL1/ABL1* for those in heart failure was 81.9% and that for those not in heart failure was 35.7% (P = 0.037).

3.4.6 Lymphadenopathy (n = 99)

The median interquartile (IQR) ranges were as follows: for initial total WBC count for those who had lymphadenopathy it was 218 and that for those who did not it was 263.5 (P = 0.562). That for initial platelet counts among those positive was 173 and that for those who were not it was 309 (P = 0.056). For initial haemoglobin for those who had lymphadenopathy it was 8.9 and that for those who did not it was 8.8 (P = 0.641).The value for initial absolute neutrophil count among those positive was 29.5 and that for those who were not it was 140 (P = 0.35). For baseline bone marrow blasts for those who had lymphadenopathy it was 3 and 4 for those who did not (P = 0.677). The values for initial *BCR:ABL1* for those who were positive was 38% and 56% for those who were not (P = 0.365).

4. Discussion

The mean age of patients in this study was 40, a reflection of the young population of Kenya whose median population was 20.1 years as per 2020 estimates. Interestingly, our study not only presented with a particularly low median age (which, as mentioned, may per se reflect the lowed median age in the population) but also found higher *BCR:ABL1* levels in younger patients. The latter finding might indeed reflect, by contrast, differences in the disease biology/onset that may warrant further investigation.

CML is characterized by the consistent presence of the Philadelphia chromosome and the *BCR:ABL1* fusion gene which derives from the reciprocal translocation: t(9;22)(q34;q11) between chromosomes 9 and 22 [8-10]. In almost all CML patients the breakpoint in the BCR gene involves the major breakpoint cluster region (M-bcr). The position of the breakpoint within the M-bcr, after exon b2 (e13) or exon b3 (e14) determines two main types of the fused *BCR:ABL1* mRNA defined as b2a2 and b3a2 transcripts which differ by 75 nucleotides. These transcripts encode two 210-k-Da tyrosine kinase proteins (P210 *BCR:ABL1*) which differ by 25 amino acids respectively [11,12].

The clinical presentation of CML is often linked to peripheral blood counts of various haematopoietic cell lines. Splenomegaly has been taken as synonymous with CML, though its rate is declining over the years because of improvements in health care, with patients being diagnosed before overt symptoms [2,5,13]. In this study, it presented significantly more commonly among males than females (p = 0.015). It has been attributed to high white blood cells in circulation.8 There was a trend in our study for those with high total white cell counts to present with splenomegaly, but this was not statistically significant (p=0.17). This is unlike in the study by Savage and colleagues among a young cohort of patients referred to the clinic for bone marrow transplant, the total white cell counts correlated directly with spleen size, and inversely with the haemoglobin level [2].

Priapism is a presentation in about 1.5% of cases. In this study, it occurred in 0.7% of the patients; however, the absolute numbers being too small for comparative and subgroups analysis. Priapism has been attributed to hyperleukocytosis, pressure on the abdominal veins by splenomegaly, or infiltration of sacral nerves by leukaemic cells [2]. Though it is a rare manifestation of CML, it is one of the most devastating, since it affects younger males more, being irreversible in up to 50% of the cases. These young people usually have not established families, yet the complication can be prevented with prompt recognition and treatment of CML.

Blindness and deafness presented in 1.4% of patients, again being rare but also devastating, requiring that CML be diagnosed and treated promptly. They have mainly been attributed to marked leukocytosis, at times retinal infiltration [5,6]. The numbers in our study were too few for subgroup correlative analysis, and are overall in line with previous findings [5,6].

Patients with high white cell numbers in circulation were likely to have symptoms that were not clearly defined [2]. The initial total white blood cell counts, and *BCR:ABL1*

levels were significantly higher among younger patients (p=0.036, and 0.025 respectively). Clinically, this didn't seem to correlate with treatment response or the need for a different management.

Younger patients also had higher *BCR:ABL1/ABL1* values at diagnosis, and also higher absolute neutrophil counts in circulation, and this has not been reported in any previous study [14]. This could reflect more brisk haematopoietic activity in younger patients. Younger patients were also more likely to be in heart failure at presentation. This was not expected since it is older patients who tend to have significant cardiac comorbidities, has never been reported before, and definitely warrants further investigation.

Lymphadenopathy was more likely to occur among patients with lower absolute neutrophil counts in circulation. This is interesting because lymphadenopathy in CML has been attributed to advanced disease with extramedullary haematopoiesis [2]. The presence of secondary myelofibrosis with cytopenias may be associated with extramedullary haematopoiesis and by extension, in lymphnodes.

Savage and colleagues found lymphadenopathy only in three patients with advanced disease [2]. In this study 8 of 99 patients evaluable (8%) had lymphadenopathy, and were more likely to have lower baseline absolute neutrophil counts (p=0.035). Liu et al attributed this occurrence to synchronous other malignancy, whereas Inverardi et al. and Woodson et al. attributed it to extramedullary haematopoiesis in blastic transformation [15-17].

In our study, patients with high platelets in circulation were more likely to present with leg swellings including nodular swellings under the skin. Such patients had significantly lower *BCR:ABL1* levels (p=0.005). In a few instances, a bloody fluid was collected from the swelling without clear evidence of clotting or hematoma formation. This finding was never described before and certainly warrants further investigations.

In a study by Balatzenko and colleagues on *BCR:ABL1* mRNA, among patients in early chronic phase, platelet counts were higher in b3a2+ patients [18]. The same were found in studies by Inochuki and colleagues, and Perego and colleagues [19,20].

Patients presenting in heart failure independent of haemoglobin levels had significantly higher *BCR:ABL1* levels at baseline compared with those who did not (p=0.037). These patients were likely to be younger, and have higher baseline white cell counts. This is a scenario that favours hyperviscosity and systemic venous thromboembolism, in a similar fashion to what happens in sickle cell anaemia [21] or direct congestive heart failure. Away from congestive heart failure due to anaemia and possibly hyperviscosity, other published data associate heart failure in CML with the use of tyrosine kinase inhibitors [22,23]. So far, a higher incidence of HF was never observed in younger patients and never directly related to *BCR::ABL1* levels.

Elderly patients have many comorbidities that include cardiovascular disease. In this study however, it was patients aged ≤20 years who were more likely to be in heart failure at presentation (P = 0.032). The relationship between *BCR:ABL1* levels at diagnosis, high neutrophils counts, young age and heart failure at diagnosis of CML has not been previously described and it's clinical basis are not clear. We may speculate that the higher *BCR:ABL1* and WBC levels are associated with an overall more serious disease that affected organs as well. It is not documented how BCR::ABL1 fusion protein may affect (directly or indirectly) heart function and functional studies are indeed warranted [24]. On the other hand, CML, as other myeloproliferative disorders, can be associated with an increased thrombotic risk. The presence of thrombosis, in this study, was not associated with other cardiac events, such as HF.

However, caution is needed when interpreting BCR:ABL1 quantitative values, because the tests are not standardized between laboratories in Kenya, and in our set-up, there are many unqualified laboratories purporting to carry out *BCR:ABL1* assays. The reliability of some of these reports is in doubt. There have been attempts to standardize *BCR:ABL1* reporting [25,26], but these have not been uniformly flawless in our setting [27]. Furthermore quantitative *BCR:ABL1* assays are not mandatory part of diagnostic work-up for CML [28]. Our situation however is unique in that, because most patients can't afford, we omit chromosome banding cytogenetics and fluorescence in-situ hybridization and go straight to quantitative *BCR:ABL1* PCR assays for diagnostic purposes, thereby obtaining reasonable assessment of baseline *BCR:ABL1* values.

Finally, the nature of the study didn't allow us to have all potentially relevant information. Genetic factors, lifestyle, and nutritional status may influence the clinical presentation of CML and future studies should address them. In perspective, electronic health record systems (or even only regular data quality assessments) may ensure higher standards in Kenyan medical research.

5. Conclusions

In conclusion, for the first time baseline *BCR:ABL1/ABL1* levels in CML have been correlated with young age at presentation, high absolute neutrophil counts in circulation and presence of heart failure. Since no clear clinical significance can be attributed, further studies are needed. The presence of lymphadenopathy in those with lower absolute neutrophil counts is circulation has also been documented. Various cell lines present at different stages may have different biologic properties which may impact clinical manifestations. More studies focusing on specific cell lines may be required to elucidate this further. Of note is that we did not factor in other circulating haematopoietic cells such as monocytes, eosinophils, myelocytes, metamyelocytes and bands, and even lymphocytes, to see what correlations they would also have in the clinical picture of CML.

Funding

This research received no external funding.

Ethics Approval and Consent To Participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Nairobi Hospital.

Consent for Publication

Informed consent was obtained from all subjects involved in the study that were enrolled in the Nairobi Hospital Glivec International Patient Assistance Program (GIPAP).

Data Availability Statement

Not applicable.

Acknowledgments

The Glivec International Patient Assistance Clinic at Nairobi Hospital. Prof. Pier Paolo Piccaluga is currently affiliated to the University of Nairobi (Nairobi, Kenya), and the University of Botswana (Gaborone, Botswana).

Conflicts of Interest

The authors declare no conflict of interest.

Author Contributions

Conceptualization, N.O.A.; formal analysis, investigation, and data curation, J.D.M.M., A.A.M., A.O.O., S.A.M., P.O.O., M.O., S.B.S., M.E., R.Y.B., M.M., K.O..; writing-original draft preparation, N.O.A..; writing-review and editing, P.P.P.; supervision, N.O.A.; project administration, N.O.A.; All authors have read and agreed to the published version of the manuscript.

References

[1] Wang Y, Liang ZJ, Gale RP, Liao HZ, Ma J, et al. Chronic myeloid leukaemia: Biology and therapy. Blood Reviews. 2024, 65, 101196. DOI: 10.1016/j.blre.2024.101196

[2] Savage DG, Szydlo RM, Goldman JM. Clinical features at diagnosis in 430 patients with chronic myeloid leukaemia seen at a referral centre over a 16-year period. British Journal of Haematology. 1997, 96(1), 111-116. DOI: 10.1046/j.1365-2141.1997.d01-1982.x

[3] Schemionek M, Elling C, Kamp L, Spieker T, Berdel WE, et al. Role of spleen in chronic myelogenous leukaemia: Lessons from an inducible mouse model. Blood. 2010, 116(21), 3384. DOI: 10.1182/blood.V116.21.3384.3384

[4] Litchman MA. Rheology of leukocytes, leukocyte suspensions, and blood in leukaemia: possible relationship to clinical manifestations. Journal of Clinical Investigations. 1973, 52(2), 350-358. DOI: 10.1172/JCI107191

[5] Szeto SK, Mohamed S, Tsang CW, Chan CK. Massive retinal infiltrates as the presenting sign of chronic myeloid leukemia: Clinical and imaging features of leukemic retinopathy. European Journal of Ophthalmology. 2023, 33(1), NP55-NP63. DOI: 10.1177/11206721211048792

[6] Holt JM, Gordon-Smith EC. Retinal abnormalities in diseases of the blood. The British Journal of Ophthalmology. 1969, 53(3), 145-160. DOI: 10.1136/bjo.53.3.145

[7] Othieno-Abinya NA, Mwanda OW, Maina MD, Odhiambo AO, Mwanzi SA, et al. Haematological parameters in chronic myeloid leukaemia as determinants of clinical manifestations in this disease. Journal of Clinical Oncology. 2016, 34(15 suppl), e18529. DOI: 10.1200/JCO.2016.34.15_suppl.e18529

[8] Shtivelman E, Lifshitz B, Gale RP, Canaani E. Fused transcript of ABL1 and BCR genes in chronic myelogenous leukaemia. Nature. 1985, 315(6020), 550-554. DOI: 10.1038/315550a0

[9] Deininger MW, Goldman JM, Melo JV. The biology of chronic myeloid leukaemia. Blood. 2000, 96, 3343-56.

[10] Rowley JD. Letter: A new consistent chromosomal abnormality in chronic myelogenous leukaemia identified by quinacrine fluorescence and Giemsa staining. Nature. 1973, 243(5405), 290-293. DOI: 10.1038/243290a0

[11] Verschraegen CF, Kantarjian HM, Hirsch-Ginsberg C, Lee MS, O'Brien S, et al. The breakpoint cluster region site in patients with Philadelphia chromosome-positive chronic myelogenous leukaemia. Clinical, Laboratory and prognostic correlations. Cancer. 1995, 76(6), 992-997. DOI: 10.1002/1097-0142(19950915)76:6<992::aid-cncr2820760612>3.0.co;2-l

[12] Quintas-Cardama A, Cortes J. Molecular biology of BCR:ABL1-positive chronic myeloid leukaemia. Blood. 2009, 113(8), 1619-1630. DOI: 10.1182/blood-2008-03-144790

[13] Chereda B, Melo JV. Natural course and biology of CML. Annals of Hematology. 2015, 94(Suppl 2), 107-121. DOI: 10.1007/s00277-015-2325-z

[14] Balatzenko G, Vunditini BR, Margarita G. Correlation between BCR:ABL1 transcripts and blood cell counts in chronic myeloid leukaemia- a possible influence of mdr1 gene expression. Hematology Reports. 2011, 3(1), e3. DOI: 10.4081/hr.2011.e3

[15] Liu ZH, Li SY, Bai O. Swollen lymph nodes may not be clinical manifestations of chronic myelogenous leukaemia: a case report and revision of literature. Therapeutics and Clinical Risk Management. 2017, 13, 1159-1162. DOI: 10.2147/TCRM.S147056

[16] Inverardi D, Lazzarino M, Morra E, Bernasconi P, Merante S, et al. Extramedullary disease in Ph'-positive chronic myelogenous leukaemia: frequency, clinical features, and prognostic significance. Haematologica. 1990, 75(2), 146-148. PMID: 2358205

[17] Woodson DL, Bennett DE, Sears DA. Extramedullary blastic transformation of chronic myelocytic leukaemia. Archives of Internal Medicine. 1974, 134(3), 523-526. DOI: 10.1001/archinte.1974.00320210133020

[18] Balatzenko G, Vunditini BR, and Margarita G. Correlation between the types of BCR:ABL1 transcripts and blood cell counts in chronic myeloid leukaemia - a possible influence of mdr1 gene expression. Hematol Rep 2011;3(1):1-4. DOI: 10.4081/hr.2011.e1.

[19] Inokuchi K, Inoue T, Tojo A, Futaki M, Miyake K, et al. A possible correlation between the type of BCR:ABL1 hybrid messenger RNA and platelet count in Philadelphia-positive chronic myeloid leukaemia. Blood. 1991, 78(12), 3125-3127. PMID: 1742479

[20] Perego RA, Costantini M, Cornacchini G, Gargantini L, Bianchi C, et al. The possible influences of B2A2 and B3A2 BCR:ABL1 protein structure on thrombopoiesis in

chronic myeloid leukaemia. European Journal of Cancer. 2000, 36(11), 1395-1401. DOI: 10.1016/s0959-8049(00)00128-3

[21] Piccin A, Fleming P, Eakins E, McGovern E, Smith OP, et al. Sickle cell disease and dental treatment. Journal of the Irish Dental Association. 2008, 54(2), 75-79. PMID: 18578383

[22] Zureigat H, Mohamed AN, Alchirazi MA, Foster P, Elghoul Y, Dhakal A, et al. Cardiovascular profile of tyrosine kinase inhibitors in chronic myeloid leukemia: A 16-Year observational study. Blood. 2024, 144, (supplement 1). :DOI: 10.1182/blood-2024-222146

[23] Berisha A, Placci A, Piccaluga PP. Cardiotoxicity of Tyrosine Kinase Inhibitors in Philadelphia-Positive Leukemia Patients. Hemato. 2023, 4(1), 68-75. DOI: 10.3390/hemato4010007

[24] Gu A, Li JT, Li MY, Liu YB. Patient-derived xenograft model in cancer: establishment and applications. MedComm. 2025, 6(2), e70059. DOI: 10.1002/mco2.70059

[25] Radich J, Yeung C, Wu D. New approaches to molecular monitoring in CML (and other diseases). Blood. 2019, 134(19), 1578-1584. DOI: 10.1182/blood.2019000838

[26] Brandford S, Fletcher L, Cross NC, Muller MC, Hochhaus A, et al. DesirABL1e performance characteristics for BCR:ABL1 measurement on an international reporting scale to allow consistent interpretation of individual patient response and comparison of response rates between clinical trials. Blood. 2008, 112(8), 3330-3338. DOI: 10.1182/blood-2008-04-150680

[27] Riaz MA, Abubakar M, Ayyoub R, Khan AN, Hameed Y. Expression Analysis of Caspase-3 (CASP3) Gene in Leukemia Patients Using Quantitative Polymerase Chain Reaction (qPCR) and Western Blot Techniques. Journal of Cancer Biomoleculars and Therapeutics. 2024, 1(2), 10–16. DOI:10.62382/jcbt.v1i2.17

[28] Archer KJ, Fu H, Mrózek K, Nicolet D, Mims AS, et al. Improving risk stratification for 2022 European LeukemiaNet favorable-risk patients with acute myeloid leukemia. The Innovation. 2024, 5(6), 100719. DOI: 10.1016/j.xinn.2024.100719

Supplementary Table 1. Association between baseline clinical signs and laboratory values

Symptom	**Results**			
Pallor	**No (n=56)**	**Yes (n=51)**	**Total (n=107)**	**P value.**
Baseline total WBC count Median(IQR)	223 (111.5,426.5)	267 (198.5,450.5)	218 (128,345)	0.301
Baseline platelet count Median(IQR)	336 (189.5,486)	288 (168,394)	303 (194.8,460)	0.135
Baseline haemoglobin Median(IQR)	9 (7.6,10.4)	8.7 (7.5,9.6)	9.4 (7.9,11.2)	0.446
Baseline absolute neutrophil count Median(IQR)	127 (55,247)	152 (58.5,239.5)	120.8 (62.8,214)	0.727
Baseline bone marrow blasts Median(IQR)	4 (2.8,5.2)	4 (4,5)	5 (3,6)	0.745
BCR:ABL1 mean(SD)	63.8 (34.7)	47.6 (35.6)	50 (34.2)	0.025
Splenomegally	**No (n=17)**	**Yes (n=90)**	**Total (n=107)**	**P value.**
Baseline total WBC count Median(IQR)	188.5 (110,341)	280.5 (174.2,448)	218 (128,345)	0.17
Baseline platelet count Median(IQR)	298.5 (234.2,377)	301.5 (173,453)	303 (194.8,460)	0.815
Baseline haemoglobin Median(IQR)	9.2 (7.9,11.5)	8.6 (7.4,9.7)	9.4 (7.9,11.2)	0.164
Baseline absolute neutrophil count Median(IQR)	113.7 (50.8,221.8)	136.5 (55,243.8)	120.8 (62.8,214)	0.951
Baseline bone marrow blasts Median(IQR)	4 (2,5.5)	4 (3,5)	5 (3,6)	0.548
BCR:ABL1 mean(SD)	63.5 (28.6)	55.2 (37.2)	50 (34.2)	0.383
Wasting	**No (n=94)**	**Yes (n=13)**	**Total (n=107)**	**P value.**
Baseline total wbc count Median(IQR)	260 (170,440)	267 (145,452)	218 (128,345)	0.935
Baseline platelet count Median(IQR)	290 (173,435)	336 (288,526)	303 (194.8,460)	0.242
Baseline haemoglobin Median(IQR)	8.7 (7.4,10)	8.9 (7.7,9.4)	9.4 (7.9,11.2)	0.859
Baseline absolute neutrophil count Median(IQR)	128 (32,243)	163 (111,312)	120.8 (62.8,214)	0.183
Baseline bone marrow blasts Median(IQR)	4 (3,5)	5.5 (3.5,8)	5 (3,6)	0.42
BCR:ABL1 Median(IQR)	56 (32.8,86.2)	39 (13,86.5)	38 (22,82.8)	0.37

Leg swelling	**No (n=93)**	**Yes (n=14)**	**Total (n=107)**	**P value.**
Baseline total wbc count				
Baseline total wbc count Median(IQR)	254 (165.4,448)	308 (190.5,427)	218 (128,345)	0.55
Baseline platelet count Median(IQR)	291 (173.8,436.2)	310.5 (189.2,497)	303 (194.8,460)	0.819
Baseline haemoglobin Median(IQR)	8.8 (7.6,9.9)	8.7 (6.6,9.4)	9.4 (7.9,11.2)	0.523
Baseline absolute neutrophil count Median(IQR)	127.5 (38.8,242.2)	165 (115.5,282.5)	120.8 (62.8,214)	0.172
Baseline bone marrow blasts Median(IQR)	4 (3,5)	4.5 (4,5)	5 (3,6)	0.328
BCR:ABL1 mean(SD)	60.5 (36)	31 (22.1)	50 (34.2)	0.005
Heart Failure	**No (n=97)**	**Yes (n=10)**	**Total (n=107)**	**P value.**
Baseline total wbc count				
Baseline total wbc count Median(IQR)	247 (163.9,404)	378.5 (261.8,507)	218 (128,345)	0.145
Baseline platelet count Median(IQR)	313 (183.8,445)	234 (111.8,290)	303 (194.8,460)	0.113
Baseline haemoglobin Median(IQR)	8.8 (7.7,9.8)	8.1 (6.9,9.9)	9.4 (7.9,11.2)	0.661
Baseline absolute neutrophil count Median(IQR)	132.5 (56.5,245.5)	135 (0,240.8)	120.8 (62.8,214)	0.701
Baseline bone marrow blasts Median(IQR)	4 (3,5)	5.5 (3.2,7.5)	5 (3,6)	0.733
BCR:ABL1 mean(SD)	54.4 (35.7)	81.9 (28.9)	50 (34.2)	0.037
Lymphadenopathy	**No (n=99)**	**Yes (n=8)**	**Total (n=107)**	**P value.**
Baseline total wbc count				
Baseline total wbc count Median(IQR)	263.5 (167,448)	218 (152.8,360.2)	218 (128,345)	0.562
Baseline platelet count Median(IQR)	309 (189.2,453)	173 (163.2,225.8)	303 (194.8,460)	0.056
Baseline haemoglobin Median(IQR)	8.8 (7.4,9.9)	8.9 (8.4,9.8)	9.4 (7.9,11.2)	0.641
Baseline absolute neutrophil count Median(IQR)	140 (58,248.5)	29.5 (0,103.2)	120.8 (62.8,214)	0.035
Baseline bone marrow blasts Median(IQR)	4 (3,5)	3 (3,7)	5 (3,6)	0.677
BCR:ABL1 median (IQR)	56 (30.5,86.5)	52 (4.2,65)	38 (22,82.8)	0.365
Other Findings	**No (n=68)**	**Yes (n=39)**	**Total (n=107)**	**P value.**
Baseline total wbc count				
Baseline total wbc count Median(IQR)	223 (145.8,399.5)	308 (174.5,461)	218 (128,345)	0.147
Baseline platelet count Median(IQR)	321 (188.5,466)	290 (171.5,384.5)	303 (194.8,460)	0.281
Baseline haemoglobin Median(IQR)	8.8 (7.5,9.9)	8.5 (7.2,9.8)	9.4 (7.9,11.2)	0.709
Baseline absolute neutrophil count Median(IQR)	128 (55,236.5)	135 (44.5,274)	120.8 (62.8,214)	0.854
Baseline bone marrow blasts Median(IQR)	4 (3,5)	4 (3,5.8)	5 (3,6)	0.798
BCR:ABL1 mean(SD)	60.1 (37.3)	50.2 (32.5)	50 (34.2)	0.189