Original Research article

Real-World Care Gaps and Survival Outcomes in Chronic Lymphocytic Leukaemia: A 20-Year Retrospective Cohort Study from Nigeria

Abstract

Background: Chronic lymphocytic leukaemia (CLL) outcomes in low-resource settings are shaped not only by disease biology, but also by delayed diagnosis, limited access to therapeutic options, and treatment interruptions due to social and financial reasons. However, data describing these real-world care gaps in sub-Saharan Africa remain limited. We evaluated the pattern of presentation, treatment access, and outcomes in CLL patients at a tertiary hospital in Nigeria.

Methods: This was a twenty-year retrospective cohort study. The demographic, clinical, laboratory, treatment, outcome and source of funding records were extracted from the patients' folders. Data was analyzed using SPSS® version 26. Overall survival (OS) was estimated using the Kaplan–Meier method, with censoring at last contact for patients alive or lost to follow-up.

Results: A total of 46 patients were included in the study. Median age at diagnosis was 53 years (IQR 49.3 – 61.5), and females were slightly more affected (n=24; 52.2%), giving a male-to-female ratio of 1:1.1. The median WBC was 81.9 $\times 10^9$/L (IQR: 53.6 – 121.0 $\times 10^9$/L), anaemia was common (n=30, 65.2%), with 9

patients (19.6%) having severe anaemia while 11 cases (23.9%) had thrombocytopenia. Staging showed 35 (76.1%) presented in Rai stage III–IV and 25 (54.3%) in Binet stage C. Overall, 38 (82.6%) received treatment, the most commonly prescribed regimens were CP (n=13, 28.3%) and CyP (n=7, 15.2%). Only 6 patients (13.0%) received a rituximab-based regimen. The overall response rate was 50%. Majority, n= 43 (93.5%) financed their treatment out-of-pocket. At last contact, 22 (47.8%) patients had died, 20 (43.5%) were lost to follow-up, while 3/46 (6.5%) were alive. The median observed OS was 16.0 months. Treated patients had a significantly longer median OS than untreated patients (17.0 vs 2.5 months; log-rank $p < 0.001$).

Conclusions: This study highlights substantial real-world care gaps in CLL in our environment. Patients commonly presented at late stage and had limited access to optimal therapy with poor outcomes. These findings highlight the need for earlier diagnosis, improved treatment affordability, and stronger continuity of care in resource-constrained settings.

Keywords: chronic lymphocytic leukaemia, CLL, treatment access, rituximab, Nigeria, real-world care

INTRODUCTION

Chronic lymphocytic leukaemia (CLL) is a lymphoproliferative neoplasm of mature B-cells.[1] It is the most prevalent leukaemia in the Western world.[2,3] The median age of onset globally is about 65 years, with males more affected than females.[4] Common clinical features at presentation include symptoms of anaemia, lymphadenopathy and splenomegaly; however, occasionally CLL may be an incidental finding detected on routine medical screening in asymptomatic patients.[5,6] Diagnosis of CLL requires a count of ≥5 X 10^9/L clonal B-lymphocytes (clonality confirmed by light chain restriction on flow cytometry).[1,7] Peripheral blood film shows lymphoid leukocytosis of small sized lymphocytes. The characteristic immunophenotypic pattern is CD5+, CD19+, CD23+, CD20 (dim), CD79b (dim/negative), CD200+, and weak surface Ig (usually IgM).[8]

The diagnostic pattern and treatment landscape of CLL has changed over the past couple of decades.[1,9] Treatment has gone from using of traditional chemotherapy to the use of chemoimmunotherapy and targeted therapy thus improving outcome in well-resourced countries. However, low-medium income countries (LMICs) are still behind in the management of patients due to delayed diagnosis, poor infrastructure, limited availability of novel drugs and financial barriers leading to care gaps.[10] Adequate management of CLL includes but not limited to timely referral, accurate diagnosis, disease staging and prognosis, treatment affordability and availability, supportive care, response monitoring, and follow-up care. In resource-constrained environments, gaps in the care of CLL patients may arise from breakdowns at multiple points in this continuum.

Available data from the African region shows a younger age at presentation compared to the western world, with more patients presenting with advanced disease.[11] However, there paucity of data on real-world care gaps in CLL. Such data are important not only for local practice improvement, but also for informing broader discussions around inequity in access to haematologic cancer care.

This study therefore aimed to describe the real-world care gaps in patients with CLL managed in a Nigerian tertiary hospital cohort, with emphasis on disease stage at presentation, baseline disease burden, treatment access, funding mechanisms, retention in care, and outcome.

METHODS

This was a retrospective cohort study of patients diagnosed with CLL and managed at the University of Port Harcourt Teaching Hospital, a tertiary hospital located in south-south Nigeria. Data was retrieved from case notes of patients. All CLL patients with sufficient records (including demographics, clinical, laboratory, treatment details, outcome and source of funding) who were diagnosed between July 2005 to June 2025 were included; those with insufficient data were excluded.

Advanced clinical presentation was defined as Rai stage III – IV and/or Binet stage C. Anaemia was defined as haemoglobin <10 g/dL, and severe anaemia as <7 g/dL. Thrombocytopenia was defined as platelet count <100 $\times 10^9$/L. Leukocytosis was defined as total white blood cell count >11 $\times 10^9$/L, and absolute lymphocytosis as absolute lymphocyte count >5 $\times 10^9$/L. Documented treatment was defined as receipt of at least one recorded therapeutic regimen. Patients recorded as alive or lost to follow-up at last contact were censored for survival analysis.

Data was collected using Microsoft® Excel and analyzed using SPSS® version 26. Categorical variables were summarised as frequencies and percentages. A p-value <0.05 was taken as being statistically significant. Overall survival (OS) was estimated using the Kaplan–Meier method, defined from the time of diagnosis to death from any cause or censoring at last contact. Ethical approval was be obtained from the hospital ethics committee.

RESULTS

A total of 46 patients with CLL were included in the study. The median age at diagnosis was 53.0 years (IQR 49.3–61.5), with a mean age of 54.6 ± 11.5 years. Females were slightly more affected, n= 24, 52.2% while males were n= 22, 47.8%, giving a male-to-female ratio of 1:1.1. Lymphadenopathy was present in 37 patients (80.4%), while 11 (23.9%) had splenomegaly. There were 30 (65.2%) cases with anaemia (haemoglobin <10 g/dL), while 9 (19.6%) had severe anaemia (haemoglobin <7 g/dL). All patients had lymphocytic leukocytosis with absolute lymphocyte count >5 X 10^9/L. The median WBC was 81.9 ×10^9/L (IQR: 53.6 – 121.0 ×10^9/L). Eleven (23.9%) had thrombocytopenia.

Table 1. Baseline clinical and haematologic characteristics of the cohort (N = 46)

Variable	***Value***
Age, years, median (IQR)	53.0 (49.3–61.5)
Female sex	24 (52.2)
Male sex	22 (47.8)
Rai stage III–IV	35 (76.1)
Binet stage C	25 (54.3)
Haemoglobin <10 g/dL	30 (65.2)
Haemoglobin <8 g/dL	16 (34.8)
Platelet count <100 ×10^9/L	11 (23.9)
WBC >11 ×10^9/L	45 (97.8)

Data are presented as n (%) unless otherwise stated.

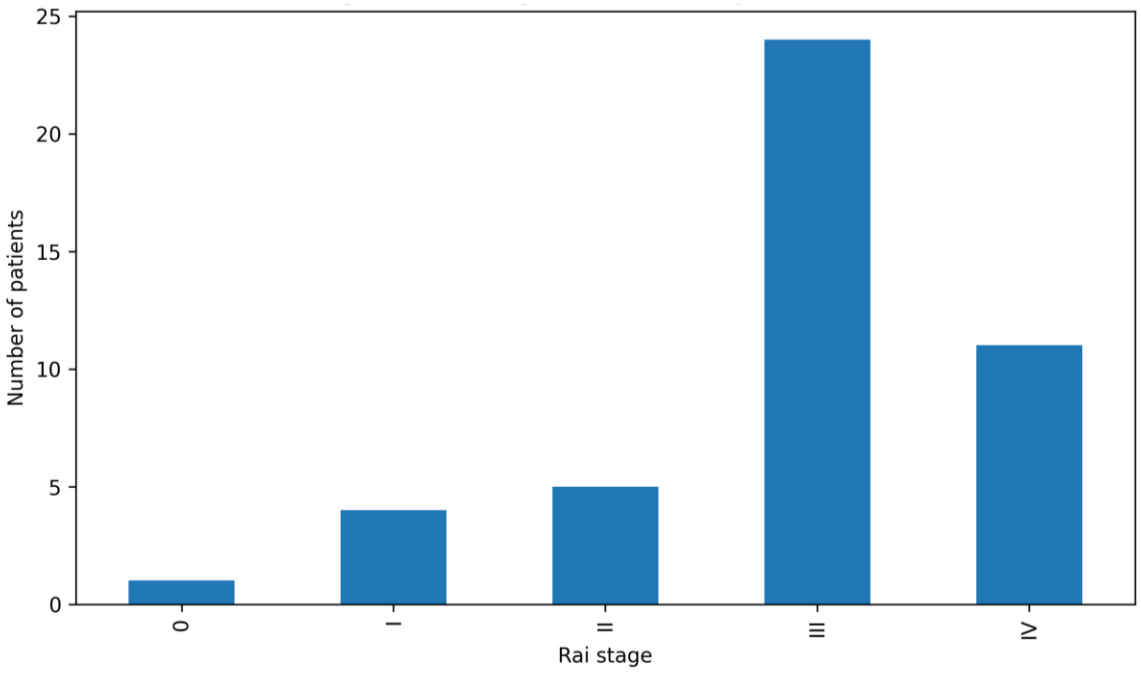

Figure 1. Rai stage distribution at presentation

Bar chart showing the distribution of Rai stage at diagnosis among patients with chronic lymphocytic leukaemia in the cohort. Most patients presented with advanced-stage disease (Rai stage III–IV), indicating delayed specialist presentation and substantial disease burden at first evaluation.

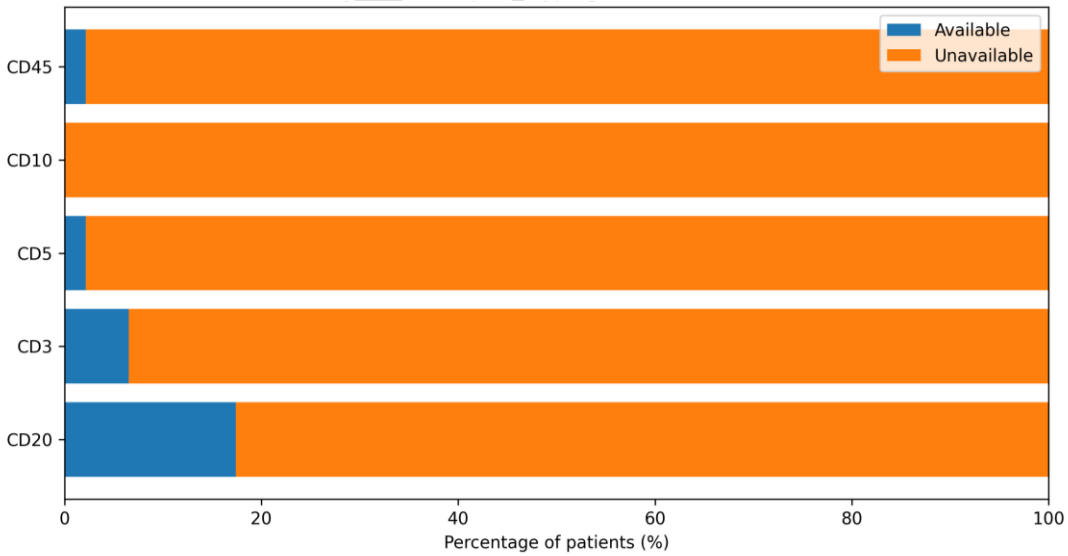

Figure 2: Availability of Immunophenotyping

Using Rai staging, 35 (76.1%) had stage III–IV disease, including 24 (52.2%) with stage III and 11 (23.9%) with stage IV disease. With Binet staging, 25 (54.3%) had stage C disease, 16(34.8%) had stage B while 4 (8.7%) had stage A disease, (see Figure 1). The CD20 status was not performed for 37 patients (80.4%), only 8 patients (17.4%) had CD20 done which was positive in all cases. CD3 results were available in only 3 patients, of whom 2 (4.3%) were negative and 1 (2.2%) was positive. CD5 and CD45 positivity were each documented in only 1 patient (2.2%) while CD10 was not done for any patient.

Overall, 38 (82.6%) received treatment while 8 (17.4%) were not treated. The most frequently prescribed regimen was chlorambucil and prednisolone (CP) in 13 (28.3%) patients, followed by cyclophosphamide and prednisolone (CyP) in 7 (15.2%), cyclophosphamide, oncovin, prednisolone (COP) was used for 5 (10.9%), and cyclophosphamide, hydroxodaunorubicin, oncovin, prednisolone (CHOP) in 4 (8.7%) cases. Two patients (4.3%) received vincristine plus prednisolone (VP). Rituximab- (R) containing or targeted regimens were less commonly used, only 6 patients (13.0%) received a rituximab-based regimen: R-ibrutinib in 3 patients (6.5%), R-CHOP in 2 (4.3%), R-COP in 1 (2.2%), and ibrutinib plus venetoclax in 1 (2.2%). With regards to funding, treatment was financed out-of-pocket in majority of patients, n = 43 (93.5%), while 2 (4.3%) had company support and 1 (2.2%) had private health insurance support.

Table 2. Treatment access and outcomes

Variable	*Value n (%)*
Received any documented treatment	38 (82.6)
Received no treatment	8 (17.4)
Out-of-pocket treatment financing	43 (93.5)
Alive at last contact	3 (6.5)
Dead at last contact	22 (47.8)
Lost to follow-up	20 (43.5)
Median time to last contact, (months)	~12
Median observed overall survival, (months)	16.0

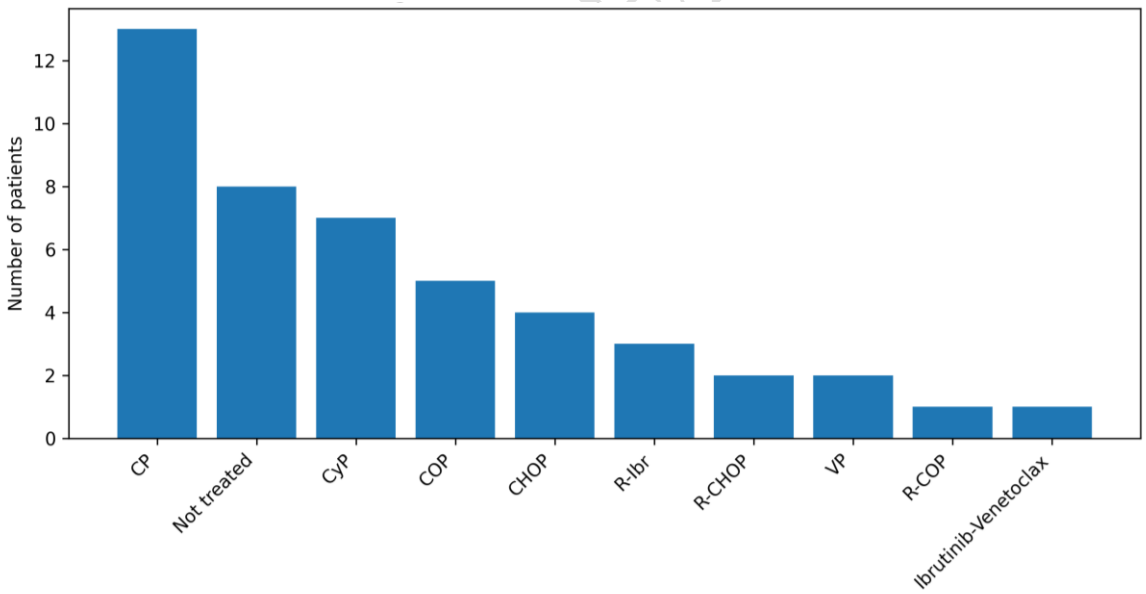

Figure 3. Treatment patterns in the cohort

Bar chart illustrating the frequency of prescribed treatment regimens. The treatment landscape was dominated by older cytotoxic or alkylator-based regimens, while use of targeted therapy was limited, reflecting constrained access to contemporary CLL treatment in routine practice.

Table 3. Distribution of prescribed treatment regimens

Treatment regimen	*n (%)*
CP	13 (28.3)
CyP	7 (15.2)
COP	5 (10.9)
CHOP	4 (8.7)
R-Ibrutinib	3 (6.5)
VP	2 (4.3)
R-CHOP	2 (4.3)
R-COP	1 (2.2)
Ibrutinib–Venetoclax	1 (2.2)

Of the 38 who received treatment, the documented overall response rate was 50.0%, with 1 patient (2.6%) achieving complete response and 18 (47.4%) achieving partial response. Ten patients (26.3%) did not respond to treatment, while there was no recorded response for 9 (23.7)% cases. At last contact, 22(47.8%) had died, 20 (43.5%) were lost to follow-up, 3 (6.5%) were alive, and outcome data were missing in 1 (2.2%). The median time from diagnosis to last recorded contact was approximately 12 months. Kaplan–Meier analysis gave a median overall survival (OS) of 16.0 months for the cohort, with estimated 6-month, 12-month, and 24-month

OS rates of 80.6%, 66.2%, and 33.6%, respectively. Treated patients had a significantly longer median OS than untreated patients (17.0 vs 2.5 months; log-rank p < .001). Estimated 12-month OS was 77.1% among treated patients compared with 0% among untreated patients. Patients who received chemotherapy had a median OS of 16.5 months, whereas those who received rituximab-containing or targeted therapy had a median OS of 65.0 months, however, this difference was not statistically significant (log-rank p = .196), likely reflecting the very small number of patients in this subgroup.

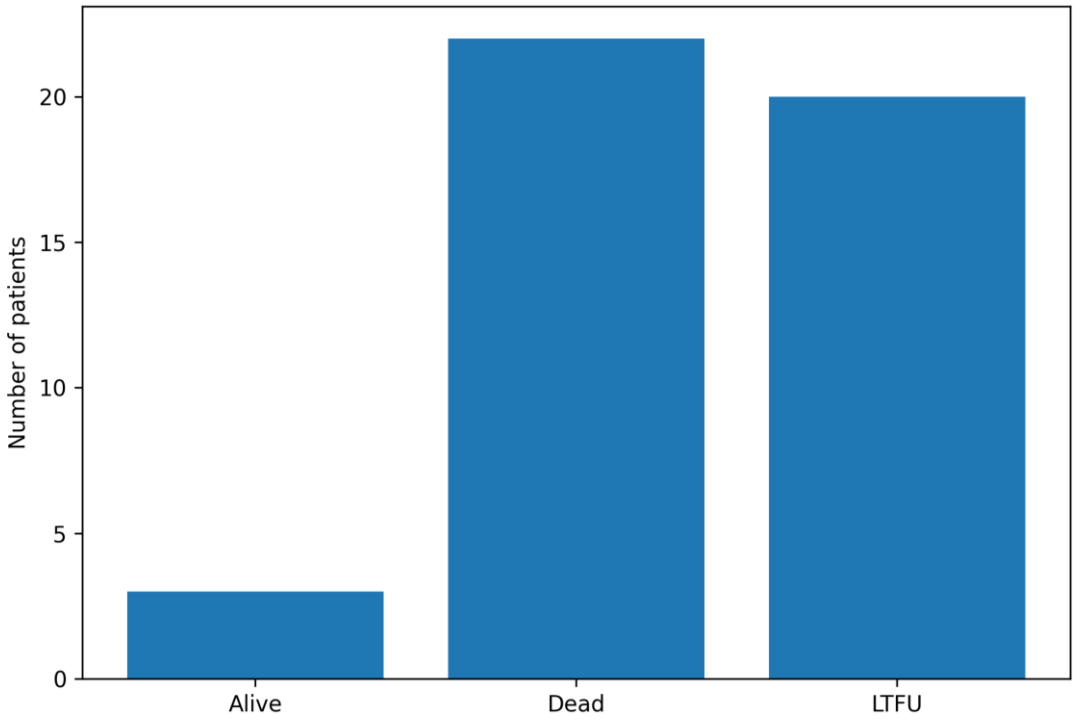

Figure 4: Patient outcomes at last contact

Bar chart showing patient status at last follow-up. A high proportion of patients had died or were lost to follow-up, highlighting the dual burden of mortality and attrition from care in this setting.

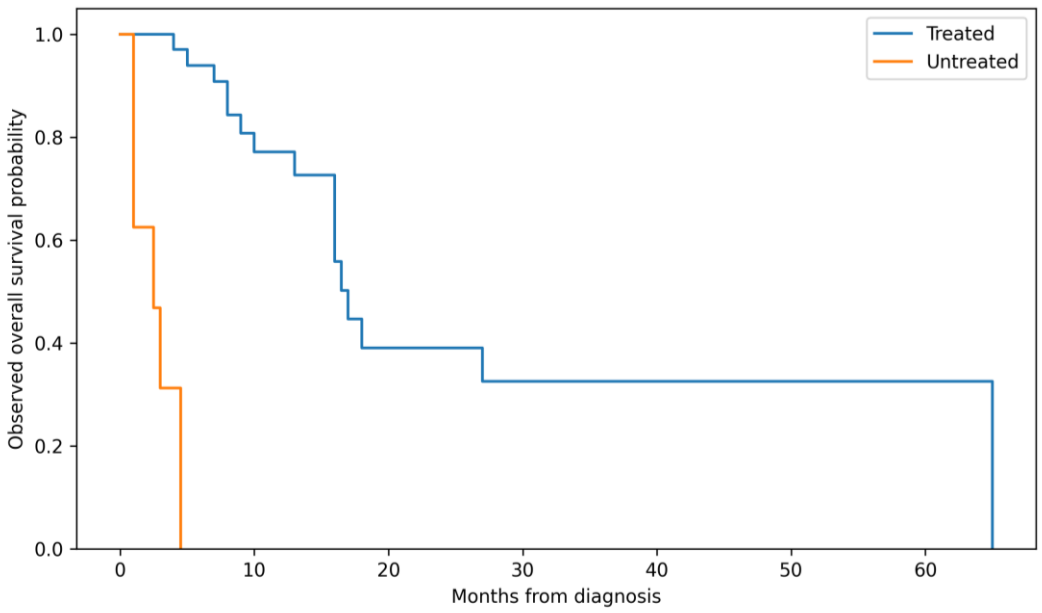

Figure 5. Kaplan–Meier survival according to treatment exposure

Kaplan–Meier curves comparing observed overall survival between patients with documented treatment exposure and those who received no treatment. Untreated patients appeared to have shorter survival; however, this comparison should be interpreted cautiously because of the small sample size, treatment-selection bias, and high rate of censoring due to loss to follow-up.

DISCUSSION

The median age at presentation of our patients was relatively younger at 53 years, unlike that reported in high-income countries where CLL is typically diagnosed in the sixth to seventh decade of life.[1,4] Similar findings of a younger age in African population have been reported by other studies[11,12].This difference in median age may be due to racial or ethnic differences, population age structure, referral patterns, and possible underdiagnosis in older populations. The younger age distribution has important implications in low-resource settings, where patients are often economically active and may face substantial financial hardship during prolonged cancer care.[13]

Over three-quarters of patients presented with advanced Rai stage III–IV disease, and more than half had Binet stage C disease, which suggests delayed diagnosis or referral to specialist care. These findings are consistent with previous Nigerian studies and underscore the importance of improving earlier diagnosis and linkage to specialist care.[11,12,14,15] There is poor health-seeking behaviour in our environment due to socio-economic factors, religious and cultural beliefs and lack of awareness. Often, many patients first seek medical attention in local pharmacies before presenting to the hospital, leading to late presentation at the hospital for care. The baseline haematologic findings further support this interpretation. There was a high prevalence of anaemia and thrombocytopenia in our patients, suggesting significant bone marrow compromise at time of presentation, although autoantibodies to red cells and platelets may also play a role in development of these cytopoenias in CLL.[16,17] The predominance of advanced disease in this cohort likely reflects gaps in early detection, limited access to diagnostic services, and barriers to timely referral.

A notable finding in this study was the marked paucity of immunophenotyping data, which highlights an important diagnostic gap in the evaluation of CLL in our environment. Immunophenotyping is central to the accurate diagnosis of CLL, but the majority of our patients did not have immunophenotyping done. CD20 status was unavailable for most patients, while CD5, CD3, CD10, and CD45 were performed for only a very small minority of cases. This reflects the limited access to flow cytometry and immunophenotypic work-up, as patients who had the test done had to have their samples shipped to an external laboratory for the test to be done thereby increasing the financial burden of performing the test due to unavailability of a flow cytometer in our centre at the time of writing this report.[18] In routine CLL practice, markers such as CD5, CD19, CD20, CD23, and light-chain restriction are essential for diagnostic confirmation and for distinguishing CLL from other mature B-cell lymphoproliferative disorders.[1,19,20] The scarcity of these data in our cohort highlights that diagnostic pathways remain constrained. This finding further underscores the broader structural limitations affecting haematologic cancer care in resource-constrained environments.

The treatment data highlights a major therapeutic access gap. Management for those who received treatment was dominated by older cytotoxic or pragmatic regimens, with very limited use of targeted therapy. Choice of therapy was largely determined by patients' ability to pay out of pocket, reflecting the strong influence of financial constraints on access to care in this resource-constrained setting. As a result, affordability played a critical role in the selection of treatment regimens. Alkylator-based and combination chemotherapy regimens dominated the treatment regimens for our patients, with only a small proportion receiving chemoimmunotherapy with rituximab-based regimens or targeted therapies. This is in contrast to management of CLL in high-income settings, where targeted agents such as ibtutinib, the Bruton tyrosine kinase (BTK) inhibitor; and venetoclax (which inhibits BCL2) have taken the frontline in treatment of CLL.[21,22,23,24] The limited use of rituximab-based regimens (13.0% in this cohort) highlights a critical therapeutic gap and suggests that access to standard-of-care treatment remains restricted.

The most striking health system finding in this study was the near-universal reliance on out-of-pocket financing, observed in over 90% of patients. In a low-medium income setting such as ours where health insurance and the awareness thereof is limited; late hospital presentation, access to diagnostics, treatment initiation, continuation of therapy, and supportive care is largely dependent on personal financial capability.[25] This financing structure likely contributes to incomplete treatment courses, and discontinuity of care. Therefore, financial toxicity is not merely a secondary consequence of cancer care but a core determinant of treatment access and outcomes.

Survival outcomes in this cohort were poor when compared to patients treated in well-resourced settings with access to newer targeted agents. The median overall survival of 16.0 months is substantially shorter than that reported in studies from high-income countries, where median survival has improved from about 3.5 years in the pre-2005 era to about 7.8 years due to the impact of BTK and BCL-2 inhibitors in the management of CLL.[26,27] Despite this poor median survival in our patients, those who did not receive treatment had a

significantly shorter survival than treated patients (2.5 vs 17.0 months, $p < .001$), suggesting that lack of access to therapy had a profound impact on outcome. This finding reinforces the importance of treatment access as a key determinant of outcomes and highlights the adverse impact of gaps in therapy availability in this setting.

Although patients who received rituximab-containing or targeted therapy in this study appeared to have longer survival than those treated with chemotherapy alone, this difference was not statistically significant. This is most likely due to the very small number of patients in the rituximab/targeted subgroup, as well as potential treatment-selection bias. However, the direction of effect seen in our patients is in keeping with already established evidence supporting improved outcomes with novel targeted drugs.

There was a high proportion of lost to follow-up cases which posed a challenge by significantly limiting the precision of survival estimates for our patients. In our low-resource setting, loss to follow-up cases often reflects underlying systemic issues such as geographic barriers as patients may have to travel a distance to access care, this is compounded by financial constraints, and health system fragmentation. Therefore, the high number of lost to follow up cases reflects gaps in the continuity of cancer care.

This study provides real-world evidence of substantial care gaps in the management of CLL patients in a Nigerian tertiary hospital cohort. The principal findings were the predominance of advanced-stage disease at presentation, a high burden of cytopenias, limited access to rituximab-based and targeted therapies, overwhelming reliance on out-of-pocket financing, and poor early outcomes characterized by high mortality and significant loss to follow-up. These findings put together suggest that the outcome of CLL in our setting is not just shaped by disease biology, but also by health system, access to care and financial constraints.

This study highlights multiple, interconnected gaps across the care continuum, including delayed presentation, limited diagnostics and access to effective therapy, financial barriers, and poor retention in care. These findings have important implications for clinical practice and health policy.

Efforts to improve CLL outcomes in similar settings should focus on strengthening early diagnostic pathways, improving access to affordable and evidence-based therapies, expanding health insurance coverage, and developing structured systems for long-term follow-up. Addressing these gaps will be essential in reducing the disparities in outcome of CLL between low- and high-resource settings.

CONCLUSION

In conclusion, this study identifies major real-world care gaps in the management of CLL in a tertiary hospital in Nigeria which included late-stage presentation, substantial baseline haematologic burden, limited diagnostics, restricted access to contemporary therapy, overwhelming dependence on out-of-pocket financing, and high attrition from care. Therefore, the burden of CLL was shaped not only by disease characteristics, but also by major deficiencies across the real-world care pathway. These care delivery failures likely contribute materially to adverse outcomes. Strengthening earlier diagnosis, financial protection, and longitudinal retention in specialist haematology care may be essential to improving survival in CLL in resource-constrained settings.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

STUDY LIMITATIONS

This study is not without limitations. Firstly, due to the retrospective design there was a lot of missing data with a high rate of loss to follow-up. Secondly this was a relatively small, single-centre cohort. Additionally, treatment allocation was not randomized, and comparisons between treatment groups are subject to confounding. Despite these limitations, this study provides valuable insights into real-world CLL care in a resource-constrained setting.

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