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Inequities in Access to Rituximab and Survival in Non-Hodgkin Lymphoma: A 20-Year Cohort Study from Nigeria

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ABSTRACT

***Background*:** Outcomes for non-Hodgkin lymphoma in sub-Saharan Africa remain constrained by delayed diagnosis, incomplete diagnosis, limited access to guideline-concordant treatment, and high out-of-pocket expenditure. Rituximab transforms outcomes in CD20-positive B-cell lymphomas, but its real-world penetration in many African oncology settings remains poorly described. We analyzed adults with non-Hodgkin lymphoma to assess treatment access, rituximab uptake, and survival outcomes.

Methods: This was a retrospective cohort study of adult NHL patients between 2005 and 2025 at two tertiary hospitals in Port Harcourt, Nigeria. Demographic, clinical, laboratory, immunophenotypic, treatment, and follow-up data were retrieved from the case notes. Data was analyzed using SPSS version 26.

***Results*:** A total of 86 patients were included. Median age was 52 years (IQR 40 - 62); 53 (61.6%) were male. Median symptom duration before presentation was 5.0 months (IQR 3.0-10.0). Among 76 (88.4%) staged patients, 40 (52.6%) had stage III/IV disease. Seventy-two (83.7%) received treatment, but only 22 (25.6%) received any rituximab-containing regimen. Among 39 patients with available CD20 testing, 37 (94.9%) were CD20-positive, of whom 21 (58.3%) received rituximab. CHOP was the most common regimen (n=41, 47.7%), followed by R-CHOP (n=18, 20.9%). Among 55 response-evaluable treated patients, objective response rate was 65.5% and complete response rate 3.6%. At last contact, 48 (56.5%) had died, 33 (38.8%) were lost to follow-up, and four (4.7%) were alive. Median overall survival for the full cohort was 12.0 months; 12-month and 24-month overall survival were 49.9% and 25.6%, respectively. Rituximab treatment was associated with superior survival (median OS 45.0 vs 11.0 months; log-rank p=0.002) and lower mortality (HR 0.32, 95% CI 0.14-0.70; p=0.005).

***Conclusion*:** Restricted access to rituximab was associated with inferior survival, highlighting treatment inequities as a key driver of avoidable mortality in NHL in low-medium income countries. Expanding access to immunochemotherapy and strengthening care systems are essential to improve outcomes.

Keywords: non-Hodgkin lymphoma; NHL; rituximab; Nigeria; sub-Saharan Africa; survival; real-world cohort

Introduction

Non-Hodgkin lymphoma (NHL) is a heterogeneous group of clonal lymphoid malignancies with major biological, pathological, and therapeutic diversity. They arise from B cells, T cells, or natural killer cells and encompass a wide spectrum of diseases with distinct molecular drivers, clinical behaviour, and therapeutic responses. Globally, B-cell lymphomas account for approximately 85–90% of non-Hodgkin lymphoma cases, whereas T-cell lymphomas constitute about 10–15%, and natural killer-cell lymphomas represent less than 5%. Non-Hodgkin lymphoma exhibits marked clinical heterogeneity, with disease behaviour ranging from indolent forms with prolonged natural history to aggressive high-grade lymphomas that require urgent treatment. Some common B-cell lymphomas include diffuse large B-cell lymphoma, follicular lymphoma, mantle cell lymphoma, and Burkitt lymphoma, each having distinct biological and clinical subtypes with varying prognoses and targeted treatment approaches. On the other hand, T-cell and NK-cell lymphomas such as peripheral T-cell lymphoma and extranodal NK/T-cell lymphoma, are typically associated with poorer outcomes and have more limited therapeutic options.[1,2] Classification of NHL is therefore based on an integrated assessment of histology, immunophenotype and cytogenetics, as recommended by the World Health Organization.[3,4] Accurate classification of non-Hodgkin lymphoma subtypes is essential not only for prognostication but also for guiding treatment selection, including the use of targeted therapies such as anti-CD20 monoclonal antibodies.[5,6]

CD20 is a non-glycosylated phosphoprotein expressed on the surface of normal and malignant B cells from the pre-B-cell stage through to mature B lymphocytes. It serves as the therapeutic target for monoclonal antibodies such as rituximab. The benefits of biologically targeted therapy in B-cell NHL is dependent on accurate diagnosis, access to CD20 testing, drug availability, and the ability to complete adequate treatment.[7] Since its approval in 1997, Rituximab (in combination with chemotherapy) has transformed the treatment landscape of B-cell NHL. In landmark randomized trials, the addition of rituximab to CHOP chemotherapy resulted in a 10–20% absolute improvement in overall survival, along with higher complete response rates and prolonged progression-free survival compared with chemotherapy alone.[8,9] More recently, newer anti-CD20 agents such as Obinutuzumab and Ofatumumab have further expanded therapeutic options in well-resourced settings.[10]

In sub-Saharan Africa, the term "NHL" still often functions as a diagnostic umbrella in our low-resource setting, reflecting deficiencies in pathology infrastructure, and incomplete access to immunohistochemistry and cytogenetics.[11,12] This diagnostic gap in our setting translates directly into therapeutic compromise, limiting prescription of appropriate targeted therapies. In addition, lymphoma care in this setting is frequently constrained by delayed diagnosis, treatment interruptions, and reduced access to chemoimmunotherapy which contribute to poorer outcomes, which are compounded by out-of-pocket financing.[13,14]

Rituximab access provides a useful indicator of equity in the management of NHL in LMICs.[15,11] Although anti-CD20 therapy should be routinely used in eligible patients, its' use is usually determined by cost rather than indication. This disconnect contributes to a widening gap between expected and observed outcomes. Evaluating rituximab uptake, particularly among patients with confirmed CD20-positive disease, offers an opportunity to quantify this implementation gap, while comparative survival analyses can estimate its clinical impact.[16] There is a paucity of longitudinal, real-world data in our setting that integrate diagnostic capacity, treatment access, and survival outcomes.

This study aimed to characterize the clinical profile of patients with NHL, quantify treatment patterns and rituximab use, evaluate response and survival outcomes, and identify factors associated with mortality. By linking diagnostic capacity, treatment access, and outcomes, this study also aims to provide actionable evidence to inform clinical practice and policy in resource-limited settings.

Methods

STUDY DESIGN AND SETTING

This was a retrospective cohort study of adult patients diagnosed with NHL managed in tertiary hospitals in Port Harcourt, Nigeria, from 2005 to 2025. Diagnosis was based on histopathological evaluation, with immunophenotyping performed where available. The study reflects real-world clinical practice in a resource-constrained setting rather than protocol-driven care.

STUDY POPULATION

Eligible patients were those aged ≥18 years with a documented diagnosis of NHL. Patients were included if clinical records contained sufficient information on diagnosis, treatment, and outcomes. Cases with incomplete diagnostic confirmation or missing data were excluded from analyses where appropriate.

DATA COLLECTION

Data were extracted from patient case notes using a structured data collection form. Variables collected included demographic characteristics (age and sex), clinical features (symptom duration and disease stage), laboratory parameters (haemoglobin, white blood cell count, platelet count, serum albumin, and creatinine), histological diagnosis and immunophenotyping (including CD20 status where available), treatment details (regimen type and rituximab exposure), and treatment outcomes. Disease staging was performed using the Ann Arbor classification where documented. Treatment response was assessed based on clinician documentation in the medical records.

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY, USA). Descriptive statistics were summarized as either mean with standard deviation for approximately symmetric continuous variables, median with interquartile range (IQR) for skewed variables, or counts with percentages for categorical variables. Baseline characteristics of treated patients who did and did not receive rituximab were compared

using Fisher's exact test or chi-square test for categorical variables and the Mann–Whitney U test for continuous variables. Overall survival (OS) was estimated using Kaplan–Meier methods with death as the event of interest. Survival curves were compared using log-rank tests. Univariable Cox proportional hazards models were fitted for age (per 10-year increase), sex, advanced stage, haemoglobin below 10 g/dL, albumin below 35 g/L, creatinine above 120 µmol/L, and rituximab exposure to assess predictors of mortality. Hazard ratios (HRs) were reported with 95% confidence intervals (CIs). A p-value <0.05 was taken to be statistically significant.

Results

There were 86 NHL patients in total. The median age was 52.0 years (IQR 40.0-62.0) with a male predominance (n= 53, 61.6%) and a male-to-female ratio of 1.6:1. The median symptom duration before presentation was 5.0 months (IQR 3.0-10.0). The distribution of NHL patients diagnosed per year is seen in Figure 1, while Figure 2 shows the histological diagnoses for the cohort. Majority (n=57, 66.3%) were diagnosed as NHL (unspecified).

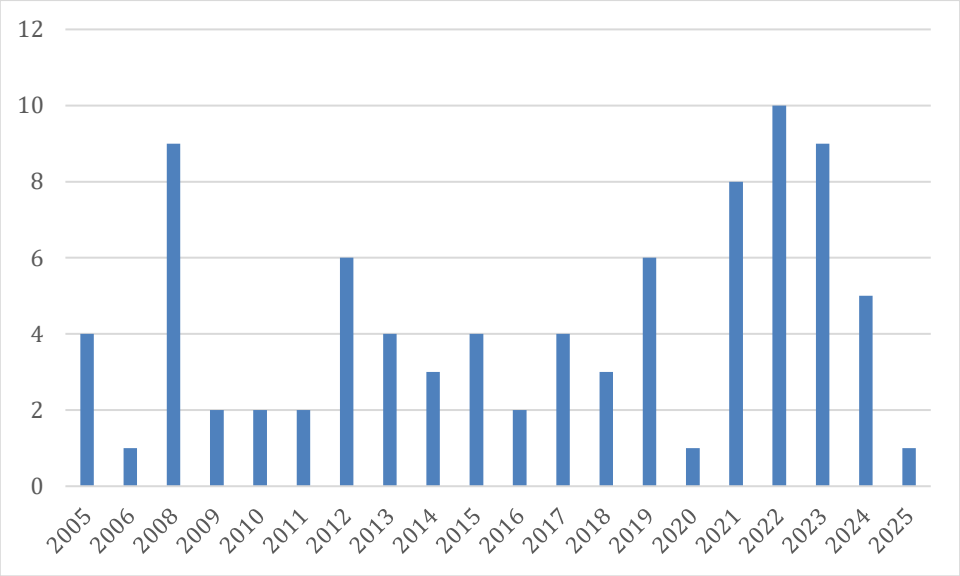

Figure 1: Number of Non-Hodgkin Lymphoma cases per year

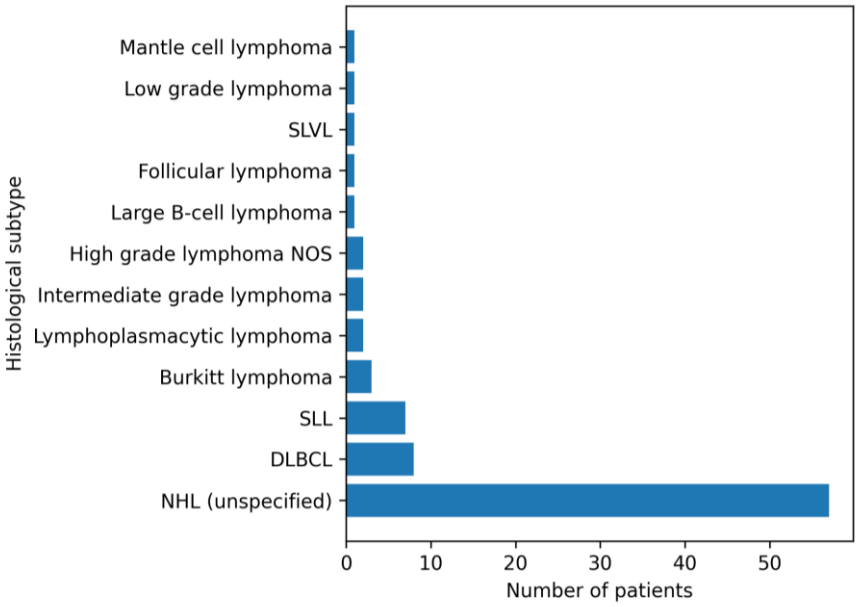

Figure 2: Histological types of Non-Hodgkin Lymphoma

Among 76 (88.4%) patients with available staging, stage distribution was: stage I, 16 (21.1%); stage II, 20 (26.3%); stage III, 16 (21.1%); and stage IV, 24 (31.6%), with advanced-stage disease (stage III/IV) accounting for over half of cases. Baseline laboratory parameters revealed: anaemia (haemoglobin concentration <10 g/dL) in 30 (34.8%); 20 (23.2%) had thombocytopoenia <100 $\times 10^9$/L. Leukocytosis (white blood cell count >11 $\times 10^9$/L) was observed in 32 (37.2%) of patients. The median white blood cell count for the overall cohort was 6.2 $\times 10^9$/L (IQR 4.5–17.4), compared with 35.7 $\times 10^9$/L (IQR 15.4–97.3) among those with leukocytosis. Hypoalbuminaemia <35 g/L was recorded in 12 of 57 patients (21.1%), while creatinine above 120 µmol/L occurred in 12 of 72 (16.7%) with the records. Immunophenotyping for CD20 was performed in 39 of

86 patients (45.3%), of which 37 (94.9%) were CD20-positive; of these only 21 (58.3%) received Rituximab-based regimen, making up 24.4% of the total cohort.

Table 1. Overall cohort characteristics.

Variable	**Value**
Total patients	86
Age, years, mean ± SD	51.9 ± 14.5
Age, years, median (IQR)	52.0 (40.0–62.0)
Male sex	53 (61.6%)
Female sex	33 (38.4%)
Duration of symptoms before presentation, months, median (IQR)	5.0 (3.0–10.5)
Known Ann Arbor stage	76 (88.4%)
Advanced stage (III/IV), among staged	40 (52.6%)
Any treatment received	72 (83.7%)
No treatment received	14 (16.3%)
Any rituximab-containing regimen	22 (25.6%)
CD20 tested	39 (45.3%)
CD20 positive	37/39 (94.9%); 37/86 (43.0%)
Rituximab received among CD20-positive	21/37 (58.3%)
Haemoglobin <10 g/dL	28/82 (34.1%)
WBC >11 $\times 10^9$/L	30/81 (37.0%)
Platelet count <100 $\times 10^9$/L	18/77 (23.4%)
Albumin <35 g/L	12/58 (20.7%)
Creatinine >120 µmol/L	12/73 (16.4%)
Dead at last contact	48 (55.8%)
Lost to follow-up	34 (39.5%)
Alive at last contact	4 (4.7%)
Follow-up, months, median (IQR)	8.0 (3.0–14.0)*

SD- standard deviation, IQR- interquartile range, WBC- white blood cell count

Seventy-one patients (83.5%) received treatment; CHOP was the dominant regimen, used in 41 (48.2%) patients, followed by R-CHOP in 18 (21.2%). COP or COP/CP-based therapy accounted for eight patients (9.4%). Figure 3 shows the treatment regimens used for those who received treatment. Other rituximab-containing regimens were uncommon and used in only two cases. Rituximab use was not observed before 2008 and remained low in the initial years after introduction (2008–2012). Although uptake increased over time, peaking in recent years, utilization remained inconsistent, with notable year-to-year variability, see Figure 3. Funding source was known for 82 patients, of whom 79 (96.3%) paid out of pocket for their care. Only isolated cases were documented as sponsored, privately insured, or company-supported.

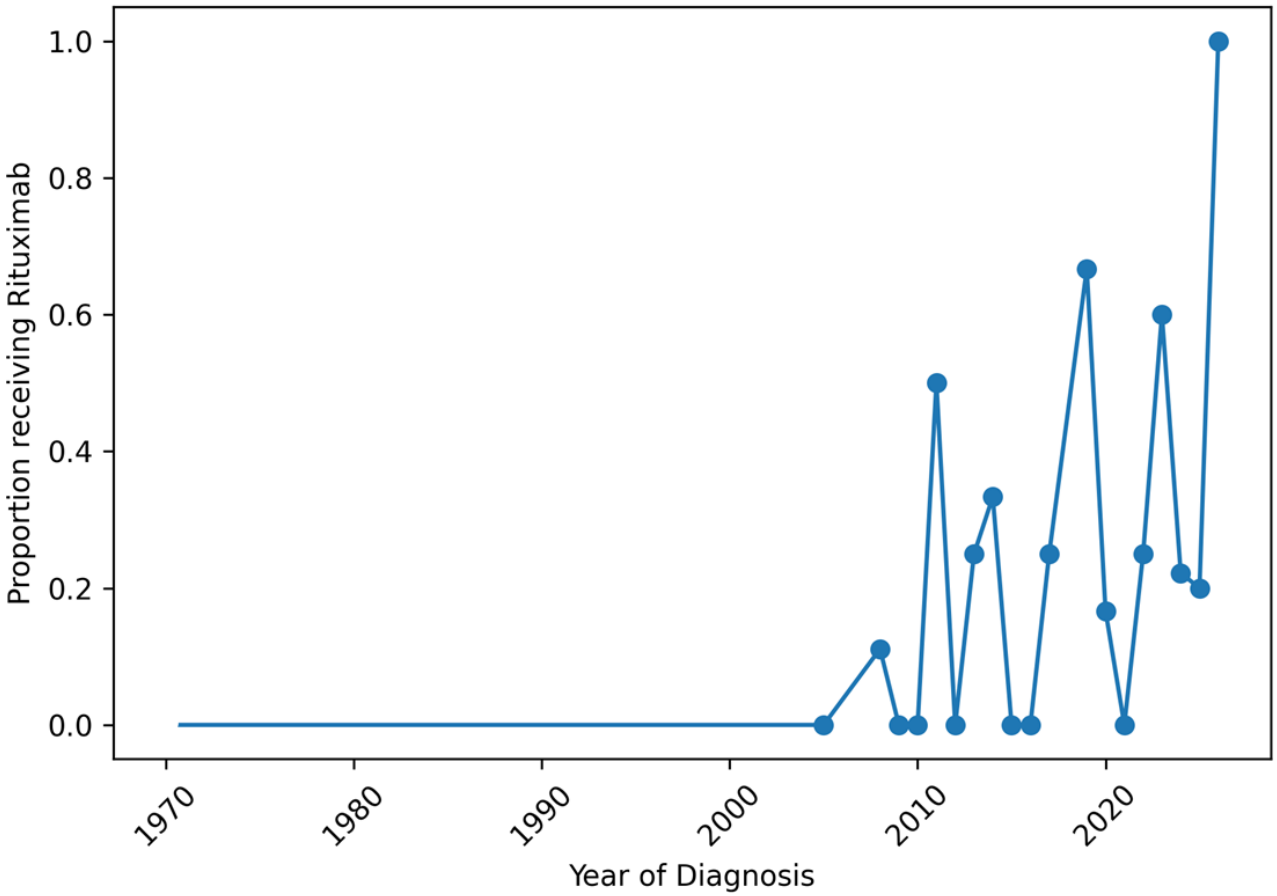

Figure 3: Rituximab Uptake over Time (2025 - 2025)

When treated patients were stratified by rituximab exposure, those who received rituximab were older than those who did not (median age 61.0 vs 50.0 years; p=0.010) and had shorter symptom duration before presentation (median 3.0 vs 8.0 months; p=0.021). Sex distribution, stage, anaemia, albumin status, and renal impairment did not differ significantly between the groups (*See Table 2*). Among the 71 treated patients, response was evaluable in 55 (77.5%) of which 36 achieved an objective response, giving an objective response rate (ORR) of 65.5%. Of the 36; only two patients achieved a complete response (3.6%), while 34 (61.8%) had partial response. Nineteen (34.5%) cases had refractory disease. Within the evaluable treated subset, objective response rate was higher among rituximab recipients (10/13, 76.9%) compared with non-recipients (26/42, 61.9%), although this difference was not statistically significant (Fisher's exact p=0.506).

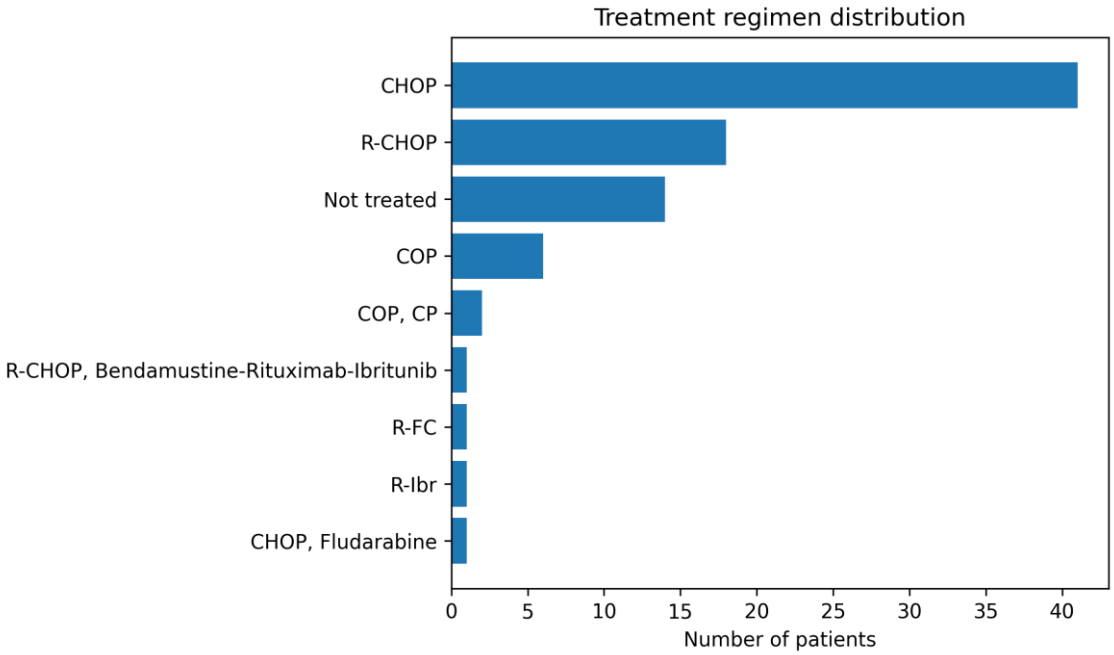

Figure 4: Treatment regimen used for patients

CHOP- cyclophosphamide, hydroxodaunorubicin, oncovin, prednisolone; R-CHOP- rituximab, cyclophosphamide, hydroxodaunorubicin, oncovin, prednisolone; COP- cyclophosphamide, oncovin, prednisolone; CP – cyclophosphamide, prednisolone; R-FC- rituximab, fludarabine, cyclophosphamide; R-Ibr – rituximab, ibrutinib

At last documented contact, 48 (56.5%) patients were dead, 33 (38.8%) were lost to follow-up, and only four (4.7%) were recorded alive. Median follow-up time was 8.0 months (IQR 3.0-14.2). Median overall survival for the entire cohort was 12.0 months. Estimated overall survival at 12 months was 49.9%, and 25.6% at 24 months. Treated patients had a median overall survival of 14.0 months compared with 2.0 months in those who were not treated (log-rank p=<0.001). Twelve-month overall survival was 53.4% in treated patients compared with 28.0% in untreated patients, this difference in overall survival was statistically significant on log-rank analysis (p=0.00024). In Cox analysis, treatment was associated with lower mortality (HR 0.22, 95% CI 0.09–0.55; p=0.001). Patients who received rituximab-containing therapy had significantly superior overall survival compared with those who did not receive rituximab, with a median OS of 45.0 versus 11.0 months; 12-month OS was 68.4% versus 41.1%, and 24-month OS was 61.6% versus 9.9% (log-rank p=0.0024). Thirty-three patients (38.8%) were lost to follow-up. Sensitivity analysis treating loss to follow-up as events rather than censoring reduced the median overall survival from 12.0 months to 8.0 months.

Table 2. Baseline characteristics of treated patients by rituximab exposure.

Characteristic	All treated (n=71)	No rituximab (n=50)	Rituximab (n=21)	p value
Age, years, median (IQR)	51.0 (40.0-62.0)	50.0 (40.0-59.8)	61.0 (52.0-67.0)	0.010
Male sex	47 (66.2%)	33 (66.0%)	14 (66.7%)	1.000
Duration of symptoms, months, median (IQR)	5.0 (2.5-10.0)	8.0 (3.0-10.0)	3.0 (2.0-5.0)	0.021
Advanced stage (III/IV), among staged	33 (51.6%)	25 (55.6%)	8 (42.1%)	0.415
Haemoglobin <10 g/dL	25 (36.2%)	19 (39.6%)	6 (28.6%)	0.427
Albumin <35 g/L	10 (20.8%)	8 (26.7%)	2 (11.1%)	0.282
Creatinine >120 µmol/L	10 (16.1%)	6 (14.6%)	4 (19.0%)	0.722

Table 3. Survival summary by treatment exposure.

Group	n	Deaths	Median OS (months)	12-month OS	24-month OS	Log-rank p
Overall cohort	85	48	12.0	49.9%	25.6%	—
Any rituximab	21	10	45.0	68.4%	61.6%	0.002
No rituximab	64	38	11.0	41.1%	9.9%	reference
Treated	71	42	14.0	53.4%	26.7%	<0.001
Not treated	14	6	2.0	28.0%	28.0%	reference

In univariable Cox analysis, rituximab exposure was associated with lower mortality (HR 0.32, 95% CI 0.14–0.70; p=0.004), *see figures 4 & 5*. Hypoalbuminaemia showed a near-significant adverse association (HR 2.61, 95% CI 0.97-7.07; p=0.059). Age, male sex, advanced stage, anaemia, and elevated creatinine were not significant in univariable models. In the multivariable model, hypoalbuminaemia (adjusted HR 3.49, 95% CI 0.90–13.50; p=0.070) and elevated creatinine 120 µmol/L; (adjusted HR 2.53, 95% CI 0.83–7.70; p=0.103) showed adverse trends, but these did not reach statistical significance.

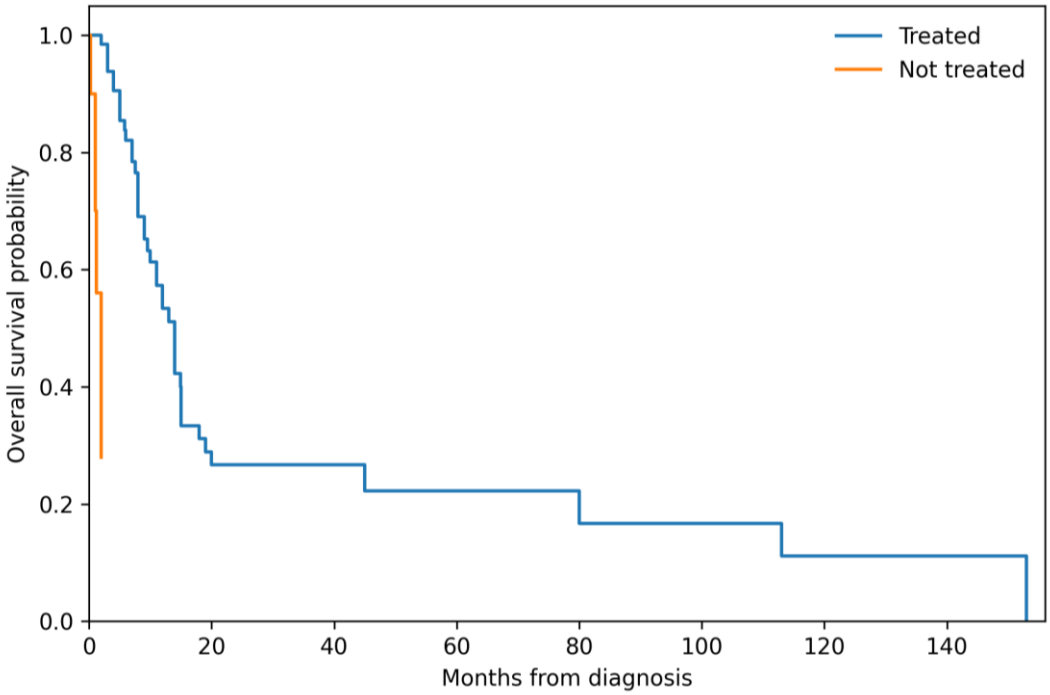

Figure 5: Overall survival comparing treated vs untreated patients

Patients who received any systemic treatment had superior survival compared with those recorded as untreated. This comparison highlights the poor outcomes associated with non-initiation of therapy.

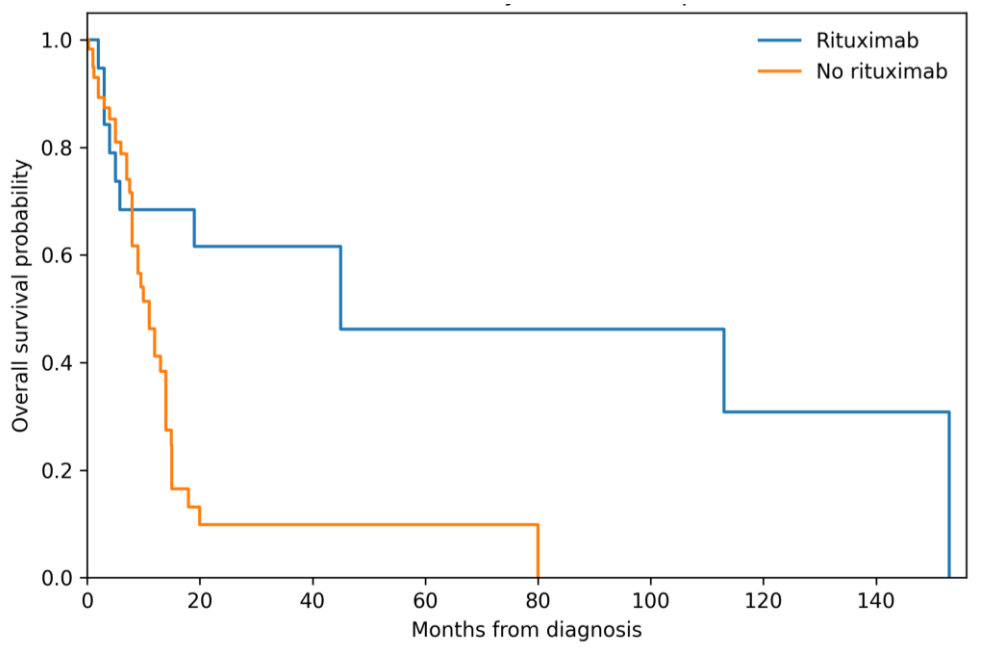

Figure 6: Overall Survival comparing patients with and without rituximab exposire

Overall survival was estimated from diagnosis to last contact, with death as the event and patients alive or lost to follow-up censored. Patients exposed to rituximab had substantially longer median overall survival than those without rituximab exposure.

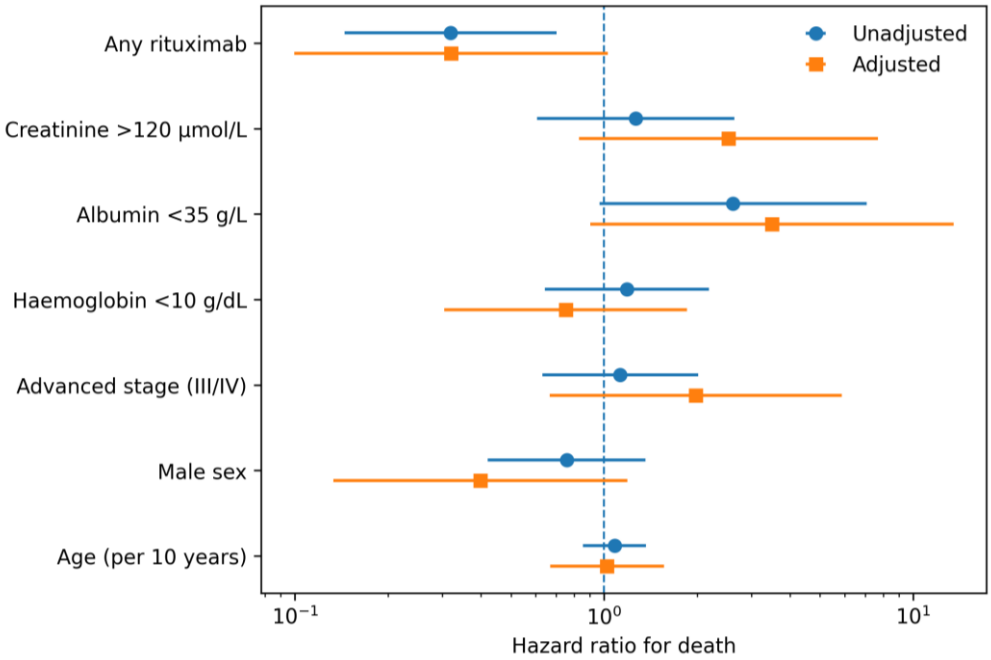

Figure 7: Predictors of mortality

Unadjusted and adjusted hazard ratios from Cox models are shown on a logarithmic scale. Rituximab exposure was associated with lower mortality, whereas hypoalbuminaemia and elevated creatinine showed adverse trends.

Discussion

The median age of 52 years and male predominance are consistent with regional data, although younger than typically reported in high-income settings.[17,18] The median symptom duration of five months before presentation underscores persistent delays in diagnosis, which may be due to poor health seeking behavior, lack of awareness, financial constraints, and inefficiencies in referral pathways.[19,20] Such delays promote disease progression prior to definitive diagnosis and commencement of treatment initiation leading to a reduced likelihood of achieving durable remission. The predominance of advanced-stage disease at presentation, with over half of staged patients in stage III/IV, supports delayed diagnosis and persistent barriers to early care in this setting.[11,21] This is further compounded by the high burden of baseline laboratory abnormalities, including anaemia, thrombocytopenia, and leukocytosis, which likely indicate a high tumour burden.[22] The marked disparity between median white blood cell count in the overall cohort and among patients with leukocytosis highlights substantial biological heterogeneity, with a subset of patients presenting with very high disease burden. Similarly, hypoalbuminaemia and increased serum creatinine in a subset of patients may suggest underlying systemic compromise, which in turn may further limit treatment tolerance and adversely affect outcomes.[23]

There was limited availability of immunophenotyping for our patients, CD20 testing performed for less than half of patients. Although the majority of those tested for CD20 were positive, only a little over half of the cohort received rituximab, representing a clear gap between biological eligibility and treatment delivery. Our findings showed that the histological diagnosis in about two-thirds of the cohort was unspecified non-Hodgkin lymphoma, reflecting diagnostic constraints due to limited facilities for further classification in our setting. Reliance on histology alone in this setting constrains clinical decision-making and likely contributes to suboptimal treatment selection.[11,12,19] Furthermore, since most patients paid out-of-pocket, financial constraints may have limited further diagnostics to determine the specific non-Hodgkin lymphoma in these patients.[24] The predominance of diagnoses of non-specific NHL in our patients highlights restricted access to immunophenotyping and advanced pathology services. In modern era of lymphoma care, subtype classification is essential for prognostication and treatment selection, especially to determine eligibility for targeted therapies such as anti-CD20 monoclonal antibodies.[25] This diagnostic gap has direct clinical consequences, as it automatically limits the number of patients that would benefit from biologically appropriate therapy. In this setting, advances in lymphoma biology and therapeutics are not fully translated into clinical practice. The consequence is a reduction in the proportion of patients who can benefit from standard-of-care immunochemotherapy, thereby contributing to poorer survival outcomes.

Twelve-month overall survival was significantly higher among treated patients compared with those who did not receive treatment (53.4% vs 28.0%), with this difference remaining statistically significant on log-rank analysis. This survival advantage was further supported by Cox regression analysis, which showed that treatment was associated with a significantly lower risk of mortality (HR 0.22, 95% CI 0.09–0.55; p=0.001), which corresponds to an approximate 78% reduction in the hazard of death. Together, these findings highlight the critical role of treatment access as a key determinant of survival in this setting. These findings highlight the critical impact of access to even basic chemotherapy in our setting and emphasizes the consequences of non-treatment. The markedly poorer survival among untreated patients may

be due to a combination of advanced disease at presentation, financial barriers to care, and health-system constraints that limit treatment initiation.

In CD20-positive B-cell lymphomas, cyclophosphamide hydroxodaunorubicin, oncovin and prednisolone (CHOP) alone is no longer considered standard of care where targeted therapy is available.[26] Majority of our patients received CHOP, which reflects poor access to immunochemotherapy rather than clinical preference. With only about one-quarter of the cohort receiving rituximab, uptake in this study was even lower than reports from other African settings, where its use in routine clinical practice often remains below 30–40%, due to both financial and health-system constraints.[11,12] Given that majority of our patients funded their treatment out of pocket, financial constraints are the most likely cause for the lower access to rituximab explanation.[27] This is in keeping with data from other low-medium income countries where cost, supply chain constraints, and lack of health insurance coverage limit access to rituximab.[11,12]

In keeping with worldwide data, those who received rituximab among our cohort had significantly better outcomes.[28] The 12-month overall survival of 68.4% seen in our patients who received rituximab is similar to findings by Kimani et al in Malawi where the 12 month OS was for diffuse large B-cell lymphoma patients who received rituximab cyclophosphamide hydroxodauno-rubicin oncovin and prednisolone (R-CHOP) was 68%. However, the 24 month overall survival of 61.6% was higher in our patients who had rituximab, compared to 55% in the same study by Kimani et al.[29]

Our patients had a poor overall survival. Median overall survival was 12 months, with fewer than one-third of patients alive at 24 months. These outcomes are in contrast to studies reported in high-income settings and are worse than those observed in better-resourced African cohorts.[30,31,32] Multiple factors which may have contributed to the poor outcome in our patients include; delayed presentation, incomplete diagnostic characterization, limited access to optimal therapy, and high rates of loss to follow-up. When lost to follow-up cases were treated as failure rather than censoring, the median survival decreased further, this suggests that mortality may likely be underestimated in the primary analysis. The objective response rate in our patients indicated a reduction in tumour burden, however the very low complete response rate seen could reflect both therapeutic limitations and inconsistencies in patient monitoring.

This study provides a real-world assessment of NHL care in a tertiary Nigerian setting and highlights the combined impact of delayed presentation, limited diagnostic capacity, constrained treatment access, and poor survival outcomes. Improving non-Hodgkin lymphoma outcomes will require better diagnostic capacity, expanded access to rituximab, and improved continuity of care, representing practical opportunities to reduce survival disparities.

Conclusion

Poor outcomes in non-Hodgkin lymphoma in this setting reflect implementation gaps rather than a lack of effective therapies. Restricted access to rituximab—despite its clear survival benefit—highlights a critical inequity in care delivery. Addressing these gaps through improved diagnostic infrastructure, expanded access to immunochemotherapy, and strengthened health systems should be prioritized to improve survival in resource-limited settings.

Study Limitations

This was a retrospective study and therefore had some missing data. There was a high rate of loss to follow-up which raises concerns about informative censoring. Treatment allocation was not randomized, introducing the possibility of confounding by socioeconomic and clinical factors.

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This study received no external funding or financial support.

Author Contributions

KIK: Conceptualization, supervision, data interpretation, manuscript drafting and revision.
EW: Data collection, statistical analysis, manuscript drafting and revision.
ADM: Data collection, literature review, manuscript drafting.
PDU: Data collection and manuscript revision.
UPO: Data collection and manuscript revision.
CAN: Supervision, data interpretation, manuscript revision.

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