

Original Research Article

Epidemiology, clinicopathological profile, treatment patterns and survival outcomes of non-Hodgkin lymphoma: a 10-year single-institution retrospective study

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ABSTRACT

Background: Non-Hodgkin lymphoma (NHL) is a heterogeneous group of malignancies with wide variation in clinical presentation and outcomes. Data from resource-limited settings on clinicopathological characteristics, treatment patterns, and outcomes remain limited.

Methods: This retrospective study included 692 patients with histologically confirmed NHL treated at a tertiary government hospital over a 10-year period. Demographic details, clinicopathological features, treatment modalities, and outcomes were extracted from medical records and radiotherapy registers using a predefined data collection form. Analyses were performed using descriptive statistics based on available data without imputation.

Results: The median age at diagnosis was 55.5 years, with a male predominance (male-to-female ratio ~1.2:1). Diffuse large B-cell lymphoma was the most common histological subtype, accounting for 56.3% of patients with documented histology. Ann Arbor staging was available in 422 patients, of whom 67.3% presented with advanced-stage disease (stage III–IV). Chemotherapy was administered in 60.1% of patients, predominantly using CHOP-based regimens. Radiotherapy was delivered with radical or consolidative intent in a substantial proportion of patients, while others received palliative radiotherapy. At last follow-up, 16.8% of patients were alive, 20.1% had died, and a significant proportion were lost to follow-up or had undocumented survival status. Kaplan-Meier survival analysis was not performed due to inconsistent documentation of follow-up dates.

Conclusions: This large single-institution study demonstrates a high burden of advanced-stage NHL at presentation in a low-resource setting, with diffuse large B-cell lymphoma as the predominant subtype. Outcomes were influenced by delayed presentation, limited access to targeted therapies, and substantial loss to follow-up. Strengthening early diagnosis, access to comprehensive oncologic care, and follow-up systems is essential to improve outcomes in similar settings.

Keywords: Non-Hodgkin lymphoma, DLBCL, Epidemiology, Treatment patterns, Survival, Retrospective study

INTRODUCTION

Non-Hodgkin lymphoma (NHL) is a heterogeneous group of lymphoid malignancies arising from B-cells, T-cells, or

natural killer (NK) cells, characterized by variable clinical presentation, histopathology, and prognosis. NHL constitutes a significant component of the global cancer burden. According to GLOBOCAN 2022 estimates, NHL

remains one of the most common haematological malignancies worldwide, with an age-standardized incidence of approximately 5.6 per 100,000 population.¹

In India, population-based registries report lower age-adjusted incidence rates compared with Western countries (approximately 2.9 per 100,000 in men and 1.5 per 100,000 in women) although data from urban centres and tertiary hospitals indicate a rising trend, likely due to improved diagnostic capabilities, greater healthcare access, increasing awareness, and changes in environmental and lifestyle factors.^{2,3}

Diffuse large B-cell lymphoma (DLBCL) is the most common histological subtype worldwide as well as in Indian populations, accounting for nearly 50-60% of cases.^{4,5} Immunophenotypic characterization plays a crucial role in subclassification, prognostication, and therapeutic decision-making. CD20 expression is observed in the majority of B-cell lymphomas and forms the biological basis for the use of anti-CD20 monoclonal antibodies such as rituximab. The addition of rituximab to CHOP-based chemotherapy has significantly improved survival outcomes in both elderly and young patients with DLBCL, as demonstrated in landmark randomized trials.^{7,18} However, access to rituximab remains inconsistent in low-resource settings due to cost constraints, leading to continued reliance on conventional chemotherapy regimens in routine clinical practice.^{6,16}

Clinical staging using the Ann Arbor system, and its modern refinements such as the Lugano classification, remains fundamental in determining treatment intent and prognosis.^{9,19,20} Early-stage disease (stage I-II) is often managed with combined modality treatment, while advanced-stage disease (stage III-IV) requires systemic chemotherapy with or without consolidative radiotherapy.^{9,19} The presence of B symptoms—defined as unexplained fever, drenching night sweats, and significant weight loss—is incorporated into staging and have been consistently associated with higher tumour burden, advanced disease, and inferior outcomes and form an integral component of prognostic models such as the International Prognostic Index (IPI).^{12,14,21}

Extranodal involvement represents an important clinical feature in NHL and has been reported in approximately 20-40% of cases.^{12,15,22} Common extranodal sites include the gastrointestinal tract, head and neck region, skin, and central nervous system.^{12,15} Extranodal disease has been associated with aggressive tumour biology, advanced stage at presentation, and treatment resistance in several studies.^{4,17}

However, resource-limited settings face challenges such as delayed presentation, restricted access to advanced diagnostics, inconsistent use of rituximab due to cost, treatment interruptions, and limited long-term follow-up, all of which may affect outcomes.^{5,7} Despite its clinical significance, region-specific data from single institutions

in India, particularly in under-represented areas, remain limited. Retrospective studies examining epidemiology, clinicopathology, treatment, and survival outcomes are essential to provide real-world evidence that can guide healthcare planning and patient management.

In this context, the present study aims to retrospectively analyse the epidemiological profile, clinicopathological characteristics, treatment patterns, and survival outcomes of adult patients with non-Hodgkin lymphoma treated over a 10-year period at a single tertiary government hospital in India, with the primary objective of characterizing the clinicopathological profile and treatment outcomes, and secondary objectives of describing histological subtypes, stage distribution, treatment patterns, extranodal involvement, and survival outcomes in the study population.

METHODS

This retrospective descriptive study was conducted in the Department of Radiation Oncology at the Regional Institute of Medical Sciences, Imphal, a tertiary-level government hospital in northeastern India that serves as a major referral centre for oncology patients, predominantly from rural and resource-limited populations. All adult patients aged 18 years or older with a histo-pathologically confirmed diagnosis of non-Hodgkin lymphoma who received treatment at the centre between January 2014 and December 2023 were included, and their medical records were retrospectively reviewed to extract demographic, clinical, treatment, and survival information.

Patients were included in the study if they had a histo-pathologically confirmed diagnosis of non-Hodgkin lymphoma, were aged 18 years or older at diagnosis, had available baseline demographic and clinical data, had WHO histological classification documented, and had received treatment during the study period. Patients were excluded if they had a diagnosis of Hodgkin lymphoma, secondary or transformed lymphomas, were referred only for second opinion or follow-up without primary diagnostic data, had records with missing key clinical or treatment information, or had duplicate entries. Data were extracted from medical records where available and included demographic and lifestyle variables such as age at diagnosis, sex, occupation, and history of alcohol and tobacco use.

RESULTS

A total of 692 patients with non-Hodgkin lymphoma were included in the final analysis. The median age at diagnosis was 55.5 years (range 18-79 years). There was a male predominance, with 377 males (54.4%) and 315 females (45.52%), yielding a male-to-female ratio of 1.19:1 among documented cases.

History of alcohol consumption was documented in a subset of patients, with 339 patients (48.98%) reporting

alcohol use and 149 patients (21.43%) reporting no alcohol use; alcohol history was not available in 204 patients (29.4%). Tobacco use was reported in 286 patients (41.38%), while 259 patients (37.42%) denied tobacco use; tobacco history was not documented in 147 patients (21.24%) (Table 1). Occupational data were heterogeneous, reflecting the real-world referral population, and were available in a subset of patients.

Table 1: Alcohol consumption history (n=692).

Variables	N	%
Alcohol use		
Yes	339	48.98
No	149	21.53
Not documented	204	29.47
Tobacco use		
Yes	286	41.32
No	259	37.42
Not documented	147	21.24

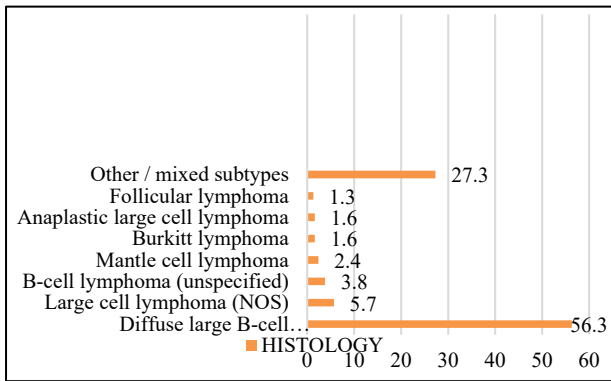


Figure 1: Histological distribution.

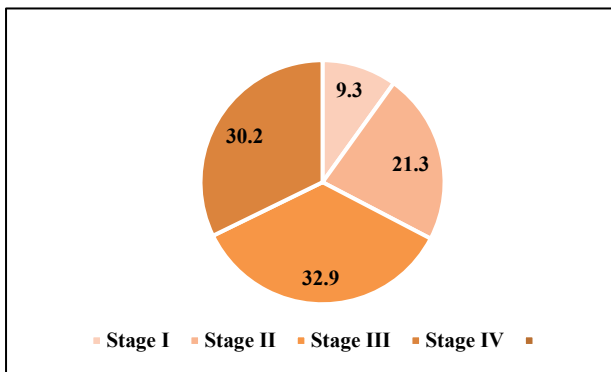


Figure 2: The stage wise distribution of non-Hodgkin's lymphoma.

Clinical and disease characteristics

Histologically, diffuse large B-cell lymphoma (DLBCL) was the most common subtype, accounting for 209 cases (56.3%) among patients with documented histology, followed by other B-cell and T/NK-cell lymphomas (Figure 1). Ann Arbor staging information was available

in 422 patients, of whom 284 (67.3%) presented with advanced-stage disease (stage III-IV) at diagnosis (Figure 2).

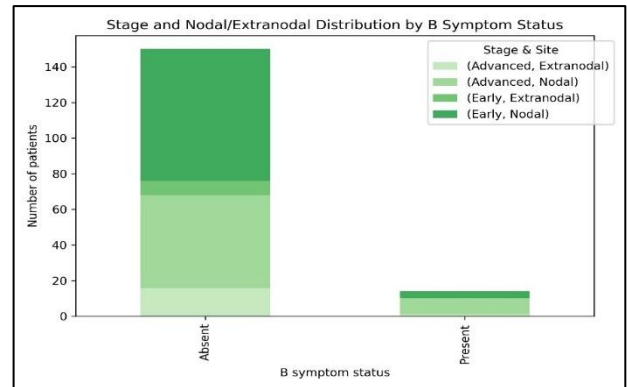


Figure 3: Stage and nodal distribution by a symptom status.

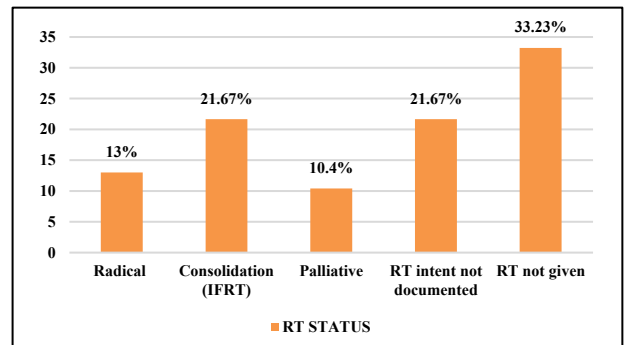


Figure 4: Distribution of patients receiving radiotherapy.

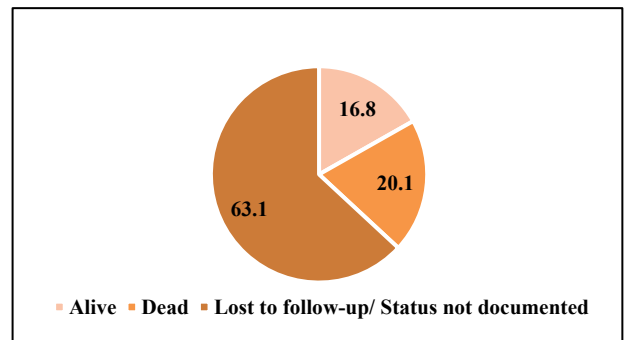


Figure 5: Survival outcomes distribution.

CD20 status was documented in 569 patients, (Table 2) of whom 459 (66.32 %) of the total cohort) were CD20-positive and 110 (15.89%) were CD20-negative; CD20 status was not recorded in 123 patients (17.77%). CD20 expression and rituximab use were analysed descriptively only due to inconsistent availability and were not correlated with treatment outcomes. Presence of B symptoms and nodal/extranodal status were further analysed. B symptoms were present in a proportion of patients (n=31), while a majority were asymptomatic at

presentation (n=310) along with some patients with missing data (n=120). Nodal disease constituted the predominant pattern of involvement, followed by extranodal disease and combined nodal-extranodal

presentation. Cross-tabulation demonstrated that patients with advanced-stage disease had a higher frequency of B symptoms and extranodal involvement compared to those with early-stage disease (Table 2).

Table 2: Association between nodal/extranodal involvement and disease stage.

Category	Advanced (III–IV)	Early (I–II)	Not documented
Both	24	0	49
Extranodal	20	9	23
Nodal	70	87	64
Not documented	5	20	90

Table 3: Primary induction chemotherapy in CD 20 +ve patients (documentation available).

Chemo regimen	No. of cycles	No. of patients			
		Consolidation RT not given	Consolidation RT given	RT given with palliative intent	RT given but intent unknown
R-CHOP	6-8# with interim assessment	52	20	25	15
R-mini- CHOP	6#	15	15	3	12
R-CVP	6#	20	30	13	35
R-CEOP	6#	10	5	1	19
Rituximab alone	6-12#	4	3	16	19

#number of chemotherapy cycles or cycles.

Table 4: Primary induction chemotherapy in CD 20 -ve patients.

Chemo regimen	No. of cycles (interim assessment)	No. of patients		
		Response	Progression	Intent unknown
CHOP	6-8#	22	10	10
CVP	6#	18	12	6
CEOP	6#	5	3	nil

#number of chemotherapy cycles or cycles.

Table 5: Number of relapse cases getting 2nd line chemo/salvage/palliative chemo (documentation available).

Status	Regimen	No. of cycles	No. of patients		
			Response	Progression	Lost to follow up/ expired/ palliation
Relapse/progression/ partial response/stable disease	R-ICE	3-6#	44	62	20
	DHAP	3-6#	11	7	2
	ICE	3-6#	8	16	10
	CVP in salvage settings	4-6#	3	10	3
	Gemcitabine+carboplatin	3-6#	6	1	5
Total patients		198			

#number of chemotherapy cycles or cycles.

In the diffuse large B-cell lymphoma (DLBCL) subset, similar trends were observed, with a higher proportion of patients presenting with B symptoms and extranodal involvement among those with advanced-stage disease, suggesting a more aggressive clinical behaviour in this subgroup. Presence of B symptoms and nodal/extranodal

status were further analysed in the study cohort. B symptoms were documented in a proportion of patients, while others were asymptomatic at presentation. Nodal disease constituted the predominant pattern of involvement, followed by extranodal disease and combined nodal-extranodal presentation.

Cross-tabulation with Ann-Arbor stage demonstrated that patients with advanced-stage disease had a higher frequency of B symptoms compared to those with early-stage diseases. Similarly, extranodal involvement was more commonly observed in patients with advanced-stage disease, indicating a greater disease burden at presentation (Figure 3).

In the DLBCL subset, similar trends were noted, with a higher proportion of patients presenting with B symptoms and extranodal involvement among those with advanced-stage disease. These findings suggest a more aggressive clinical profile in advanced-stage DLBCL, although formal survival analysis was not performed due to lack of reliable follow-up data.

Treatment patterns

Treatment modalities included chemotherapy, radiotherapy, or combined modality therapy. Chemotherapy was administered in 416 patients (60.1%), while 44 patients (6.4%) did not receive chemotherapy; chemotherapy status was not documented in 232 patients (33.5%). Radiotherapy was delivered with radical or consolidative intent in 240 patients (51.9%), whereas 72 patients (15.58%) received palliative radiotherapy; radiotherapy intent was undocumented in the remaining cases leading to a total of 462 (66.76%), patients receiving RT regardless of the intent with variable dosing schedules (Figure 4). There are around 34 (7.35%) patients who neither have CD 20 status documentation nor intent of RT documentation but underwent radiotherapy which probably to palliate the symptoms but were not categorised in the same to avoid data imputation. There are around 151 (21.82%) patients who had documented CD 20 status but didn't receive RT due to either good treatment response post definitive chemotherapy or lost to follow up or expiry of the patient or unknown reasons.

Chemotherapy regimens tried include R-CHOP and R-mini-CHOP, R-CVP, R-CEOP, Hyper-CVAD in the primary settings while some cases required salvage chemo where R-ICE, ICE alone, DHAP were tried. Some cases were given single agent maintenance Rituximab (Table 3). The data pertaining to whether a patient received any Radiotherapy (RT) following chemotherapy (Chemo) and the intent with which it was given was displayed in the Tables 3-5 with categorisation based on CD 20 status and the setting in which it was tried. Further analysis was again cutout in order to avoid imputation and further complications.

The most common radiotherapy dosing both in radical and consolidation was 30 Gy over 15 fractions, noted in 317 patients (68.61% of total patients receiving RT) whereas a dose of 40 Gy in 20 # was given in 54 patients, depending on the disease bulk and response to induction chemotherapy. In the remaining 19 patients different dose fractionations were tried. A total of 72 (10.4%) patients received various palliative radiotherapy doses with 30 Gy over 10 fractions being the most common.

A total of 245 patients had documented toxicities including myelosuppression, anaemia, peripheral neuropathy, mucositis, alopecia, hyperglycaemia secondary to treatment with prednisolone as a part of the chemo regimen. However, the most notorious side effect of doxorubicin i.e., cardiomyopathy, of the documented cases was seen in 11 patients only.

Patients who experienced significant toxicities such as severe myelosuppression were given some break from further chemotherapy cycles and most of the patients recovered from the adverse effects.

At last follow-up, 116 patients (16.8%) were alive and 139 patients (20.1%) had died, while 437 patients (63.1%) were either lost to follow-up or survival status was not documented (Figure 5).

Kaplan-Meier survival analysis could not be undertaken due to incomplete and heterogeneous documentation of follow-up dates, and treatment outcomes were therefore assessed based on survival status at last recorded follow-up.

DISCUSSION

This retrospective analysis of 692 patients with NHL treated at a tertiary government hospital provides a comprehensive real-world perspective on disease characteristics, treatment patterns, and outcomes in a low-resource setting. Representing one of the larger single-institution radiotherapy-based series from India, the study highlights challenges that continue to influence NHL management outside controlled clinical trial environments.

The median age at diagnosis in the present cohort was 55.5 years, which is lower than that reported in Western populations, where NHL commonly presents in the sixth to seventh decade of life. This observation is consistent with multiple Indian and South Asian studies and likely reflects differences in population demographics, environmental exposures, genetic susceptibility, and referral patterns within the region.¹²⁻¹⁴ The male predominance observed in this study mirrors global epidemiological trends and has been consistently reported across Indian institutional series.^{15,16}

DLBCL was the most frequent histological subtype, accounting for over half of patients with documented histology. This distribution aligns with global data and reinforces the dominance of DLBCL across geographic regions.^{3,16} However, a significant proportion of cases were classified under nonspecific or incompletely characterized categories, underscoring limitations in immunohistochemical profiling, particularly in earlier years of the study period. Similar diagnostic constraints have been reported from other resource-limited centres in India.^{7,17}

A notable finding of this study was the high proportion of patients presenting with advanced-stage disease. Among

patients with documented staging, nearly two-thirds had Ann Arbor stage III or IV disease at diagnosis. Late presentation remains a persistent challenge in low- and middle-income countries and may be attributed to delayed symptom recognition, limited access to diagnostic facilities, socioeconomic barriers, and referral delays.^{3,17} Advanced disease at presentation significantly influences treatment intent and contributes to poorer outcomes, as reflected by the substantial proportion of patients receiving palliative radiotherapy.

B symptoms, including unexplained fever, night sweats, and weight loss, are well-recognized adverse prognostic factors in non-Hodgkin lymphoma and form an integral component of the Ann Arbor staging system. In the present study, a substantial proportion of patients presented with B symptoms, reflecting a high tumour burden and biologically aggressive disease. Previous large epidemiological analyses have consistently demonstrated that the presence of B symptoms is associated with advanced-stage disease, higher International Prognostic Index (IPI) scores, and inferior survival outcomes.^{12,14} Our findings corroborate these observations, as patients with B symptoms in our cohort were more likely to present with advanced-stage disease, underscoring the role of systemic symptomatology as a surrogate marker of disease extent and activity.

Nodal disease constituted the predominant pattern of presentation in our cohort, followed by extranodal involvement, which is consistent with published Indian and international series.^{5,8} Extranodal non-Hodgkin lymphoma has been reported to account for 20-40% of all NHL cases globally, with the gastrointestinal tract, head and neck region, and central nervous system being common sites.^{12,15} The frequency of extranodal disease in our study reflects the heterogeneous nature of NHL and emphasizes the need for site-specific diagnostic and therapeutic approaches. Importantly, extranodal involvement has been associated with more aggressive disease behaviour, treatment resistance, and poorer outcomes in several studies.^{4,17}

Stage-wise subset analysis in our cohort demonstrated a higher prevalence of extranodal disease among patients with advanced-stage lymphoma, further highlighting the association between disease dissemination and extranodal spread. Similar findings have been reported by Sharma et al and Babu et al where extranodal involvement was significantly more common in patients with stage III-IV disease.^{16,17} In the diffuse large B-cell lymphoma subset, this trend was even more pronounced, suggesting a more aggressive clinical phenotype in advanced-stage disease. These observations reinforce the importance of early diagnosis and prompt initiation of therapy to prevent disease progression and systemic dissemination, particularly in resource-limited settings where delayed presentation remains common.

Systemic chemotherapy formed the backbone of treatment, with CHOP-based regimens being most commonly employed. Although CD20 positivity was

documented in a subset of patients, the use of rituximab was inconsistent and largely influenced by affordability and availability. This real-world treatment pattern reflects the disparity between evidence-based recommendations and actual practice in resource-constrained settings. While randomized trials have demonstrated improved survival with the addition of rituximab in CD20-positive DLBCL,¹⁸ the benefits of such targeted therapies are not uniformly realized in routine clinical practice in low-resource environments.

Radiotherapy played a significant role in disease management, delivered with radical or consolidative intent in a substantial proportion of patients and with palliative intent in others. The frequent use of moderate-dose regimens is in keeping with contemporary practice for consolidation and symptom palliation in NHL. These findings reaffirm the continued relevance of radiotherapy as an integral component of multidisciplinary NHL management, particularly for localized disease, bulky presentations, residual disease following chemotherapy, and palliation.¹⁹

Substance use history, including alcohol and tobacco consumption, was documented in a subset of patients. Although the extent of missing data precluded meaningful correlation with disease characteristics or outcomes, inclusion of these variables provides a broader clinicodemographic profile and may inform future prospective studies examining lifestyle-related risk factors in NHL.¹³

Survival outcomes were assessed using status-based measures at last follow-up. Kaplan-Meier survival analysis was not performed due to inconsistent documentation of diagnosis dates, follow-up duration, and progression events across the study period. Such limitations are well recognized in retrospective analyses from resource-limited settings.^{7,18} Additionally, a high proportion of patients were lost to follow-up, reflecting challenges related to geographic distance, socioeconomic constraints, referral-based care, and lack of structured survivorship programs. Transparent reporting of these limitations avoids overestimation of outcomes and strengthens the scientific validity of the study.

The strengths of this study include its large sample size, extended duration, and reflection of real-world clinical practice in a government tertiary care setting serving an underserved population.

Limitations include its retrospective design, heterogeneous documentation, incomplete staging and immunohistochemical data, and substantial loss to follow-up. These limitations were addressed by restricting analyses to available data without imputation and by adhering to established reporting guidelines. Due to the retrospective nature of the study and variable documentation in hospital records, all analyses were performed based on available data, and missing information was handled without imputation.

CONCLUSION

This large single-institution retrospective study highlights the real-world clinicopathological profile, treatment patterns, and outcomes of non-Hodgkin lymphoma in a low-resource tertiary care setting. Diffuse large B-cell lymphoma emerged as the predominant histological subtype, with a substantial proportion of patients presenting with advanced-stage disease at diagnosis. Chemotherapy and radiotherapy formed the cornerstone of management, with radiotherapy playing a crucial role in both curative and palliative settings. Treatment outcomes were limited by advanced disease at presentation, inconsistent access to targeted therapies, and a high rate of loss to follow-up, reflecting systemic challenges inherent to resource-constrained healthcare environments. These findings underscore the need for earlier diagnosis, improved access to comprehensive diagnostic and targeted treatment modalities, and strengthened follow-up mechanisms to improve outcomes for patients with non-Hodgkin lymphoma in similar settings.

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