Original article

Clinico-pathological Profile of Patients with Non-Hodgkin's Lymphoma

Hossain MM[1], Parveen R[2], Irshadullah NM[3], Rumi MSIS[4], Chowdhury MSZ[5], Yamani MJ[6], Mahmood T[7], *Nurunnabi M[8]

Abstract

Background: Non-Hodgkin's lymphoma (NHL) is a neoplasm affecting the lymphoid tissue. It can develop from chromosomal translocations, exposure to certain toxins, infections, or prolonged inflammation. NHL encompasses multiple subtypes, each with distinct epidemiology, immunophenotypic characteristics, genetic profiles, clinical presentations, and treatment approaches.**Objective:** The aim of this study is to explore the clinico-pathological profile of the NHL patients. **Methods:** A total of 32 patients were enrolled in this study from purposively selected two tertiary care hospitals and all necessary information was gathered using a structured questionnaire and analyzed for the findings. **Results:** Majority of the patients were over 40 years; males were the predominant gender; common characteristics included nodal presentation, B cell histologically and diffuse large B-cell lymphoma as per immunohistochemistry, staging wise Stage II and clinical features wise neck swelling; lastly nodal engagement-wise cervical lymphadenopathy and extra-nodal involvement wise being gastrointestinal tract and lung lymphadenopathy. **Conclusion:** Holistic Comprehensive knowledge of the disease progression and the involvement of a multidisciplinary team are crucial for the effective care and management of patients.

Keywords: Non-Hodgkin's lymphoma, neoplasm, clinico-pathological profile, staging, Bangladesh.

Introduction

Malignant lymphomas are a group of cancers with varying levels of malignancy, originating from lymphoid tissue cells—specifically lymphocytes or histiocytes—at different stages of development. Non-Hodgkin's Lymphoma (NHL) is one such lymphoma, representing a heterogeneous group of lymphoproliferative cancers characterized by diverse B and T cell proliferations. NHL differs significantly from Hodgkin's Lymphoma in terms of prognosis and is more likely to spread to multiple sites.[1] Globally, NHL is the most communal hematological malignancy, accounting for about 3% of all cancer diagnoses and deaths. It is more prevalent among men, individuals over 65, those with autoimmune diseases such as Sjogren's syndrome, systemic lupus erythematosus, celiac disease, and scleroderma, and those with a family history of hematological cancers. Additional risk factors include exposure to ultraviolet radiation, certain occupational hazards, and viral infections like Epstein-Barr virus, Helicobacter pylori, and Hepatitis C.[1,2] The most conjoint type of NHL is diffuse large B-cell lymphoma, followed by follicular lymphoma. Marginal zone B-cell lymphoma, Burkitt's lymphoma, mantle cell lymphoma, and NK/T cell lymphoma are some of the less frequent forms.[1]

Clinically, NHL can manifest as nodal or extranodal lymphomas. Nodal lymphomas typically present as painless cervical lymphadenopathy, often involving

Author's Affiliation:

1. Mohammed Murad Hossain, Assistant Professor, Department of Haematology, Mymensingh Medical College Hospital, Mymensingh 2200, Bangladesh.
2. Rahnuma Parveen, Assistant Professor, Department of Medicine, Shaheed Tajuddin Ahmad Medical College, Gazipur 1712, Bangladesh.
3. Naseeb Muhammad Irshadullah, Assistant Professor, Department of Haematology, Shaheed Tajuddin Ahmad Medical College, Gazipur 1712, Bangladesh.
4. Muhammad Shahidul Islam Sikder Rumi, Assistant Professor and Head, Clinical Haematology, Bangladesh Institute of Health Science (BIHS) General Hospital, Dhaka 1216, Bangladesh.
5. Md. Sazzad Zayed Chowdhury, Consultant Haematologist, Goulburn Valley Health, Victoria 3630, Australia.
6. Md. Jaki Yamani, Hematologist, University Hospitals of Leicester NHS Trust, Leicester LE1 7RH, United Kingdom
7. Tarim Mahmood, Public Health Researcher, National Institute of Preventive and Social Medicine, Dhaka 1212, Bangladesh.
8. *Mohammad Nurunnabi, Assistant Professor, Department of Community Medicine and Public Health, Sylhet Women's Medical College, Sylhet 3100, Bangladesh.

Address of Correspondence : *Mohammad Nurunnabi, Assistant Professor, Department of Community Medicine and Public Health, Sylhet Women's Medical College, Sylhet 3100, Bangladesh. nur.somch@gmail.com https://orcid.org/0000-0001-9472-9369

multiple lymph nodes. NHL frequently spreads to non-contiguous lymph nodes as well. Extranodal manifestations commonly affect Waldeyer's ring.[3] Histologically, the features of NHL can be classified as either nodular or diffuse. In the nodular pattern, neoplastic cells aggregate to form large clusters. In contrast, the diffuse pattern is characterized by a uniform distribution of cells, lacking nodularity or germinal center formation, and results in a complete effacement of the lymph node architecture.[4]

Early diagnosis and a multidisciplinary approach are essential for effectively managing the different types of NHL. The AAS Classification is commonly employed to assess the extent of the disease.[5] Accurate clinical staging involves a thorough history and physical examination, appropriate imaging of the chest, abdomen, and pelvis, blood chemistry tests, a complete blood count, and a bone marrow biopsy. Basic staging and assessment for patients with NHL typically include all of these evaluations, with imaging primarily conducted using computed tomography (CT) scans. For patients who cannot safely undergo a CT scan, MRI is often used as an alternative. Recent advancements in functional imaging, particularly with PET scans, have enhanced imaging options for NHL. Additionally, patients at high risk for central nervous system involvement should undergo a lumbar puncture for cerebrospinal fluid cytology.[6] Some drugs have demonstrated enhanced effectiveness in treating NHL. Effective management of NHL necessitates various therapeutic strategies tailored to tumor burden. Since the introduction of newer medications in combination with chemotherapy and maintenance therapy, remission and survival rates have significantly improved. Rituximab-based chemo-immunotherapy, in particular, has led to notable advancements in the outcomes for patients with diffuse large B-cell lymphoma.[7] Early-stage disease is typically treated with radiation therapy, while patients with stage III and IV disease usually receive chemotherapy, immunotherapy, or radioimmunotherapy.[8]

Methods

Study design and settings

This descriptive, cross-sectional study involved 32 clinically diagnosed cases of Non-Hodgkin's Lymphoma (NHL). Our objective was to assess the clinico-pathological profile of NHL patients in these settings, including demographic, morphological, and clinical characteristics, as well as tumor staging. The study was conducted at two tertiary-level hospitals: the first 24 cases were recorded at the National Institute of Cancer Research and Hospital (NICRH) in Dhaka from May 2019 to December 2020, while the remaining 8 cases were identified in the Department of Hematology at Mymensingh Medical College and Hospital from January 2024 to June 2024. A purposive sampling technique was employed for this study.

Sample selection criteria

The selection criteria were defined as follows: the inclusion criteria encompassed patients diagnosed with NHL based on immunohistochemistry (IHC). The exclusion criteria included patients who did not undergo IHC, and critically ill individuals with various comorbidities.

Data collection procedures

Case records were reviewed for demographic information, presenting complaints, and symptoms. The Ann Arbour system (AAS) was used to classify all cases during the initial staging phase, and the 2008 WHO classification of lymphoid neoplasms was used for histological classification. Relevant diagnostic and imaging tests were conducted. A structured questionnaire served as the research instrument, and all data were collected through face-to-face interviews and hospital records.

Ann Arbor Staging (AAS)

The AAD system was originally developed to stage Hodgkin's disease but is also applicable for the anatomical staging of NHL. The AAS classification is considered the most effective method for anatomically staging NHL and has been universally adopted for this purpose. This system categorizes patients into four stages based on the extent of the disease: localized disease, multiple sites of disease on one side of the diaphragm, lymphatic disease affecting both sides of the diaphragm, and disseminated extranodal disease. Below is an illustration of the classification.

- Stage I: Involvement of a particular lymph node area or lymphoid tissue.
- Stage II: Two or more lymph node areas on the same diaphragmatic side are involved.
- Stage III: Involvement of lymphatic areas or tissues on both sides of the diaphragm.
- Stage IV: Involvement of extra-nodal sites.[6]

ECOG Performance Status

This scale is utilized by healthcare professionals and researchers to evaluate disease progression, its impact on daily activities, and to inform prognosis and treatment options for patients. The categories are as follows: -

- Grade 0: Fully active, able to perform all pre-disease activities without restriction.
- Grade 1: Limited in physically strenuous activities but ambulatory; capable of light or sedentary work, such as light housework or office tasks.
- Grade 2: Ambulatory and able to manage all self-care, but unable to engage in any work

activities; active for more than 50% of waking hours.

- Grade 3: Capable of only limited self-care; confined to bed or a chair for more than 50% of waking hours.
- Grade 4: Completely disabled; unable to perform any self-care and totally confined to bed or a chair.
- Grade 5: Dead.[9]

Statistical analysis

After collecting all data, a screening process was conducted to exclude participants who did not meet the inclusion or exclusion criteria. Data cleaning was then performed to remove missing and extreme values, ensuring the raw data was accurate. Data analysis began once all information had been screened. Descriptive analysis was carried out using the Statistical Package for the Social Sciences (SPSS, Version 25). The results were presented in tables and charts, displaying frequencies and percentages as appropriate.

Ethical approval

Prior to the study, the thesis protocol was submitted to the Institutional Review Board (IRB) of both hospitals. This study relied solely on medical records and posed no social or legal risks to the subjects, nor did it compromise their privacy. All necessary precautions were taken to ensure that the study did not cause any harm or delays in the treatment of the cases. All data were treated confidentially, with access restricted to the investigation regulatory authority and review committee. Informed written consent was obtained from participants prior to their enrollment in the study.

Results

The table above illustrates the socio-demographic and certain clinical characteristics of the patients. Regarding age, groups of 41-60 years and greater than 60 years had the maximum participants, 10 (31.3%) in each of them. However, the age range was 17-75 years. With concern to gender, maximum, meaning 22 (68.8%) were males. Male to female ratio was 2.2:1. In context of educational status, 13 (40.6%) and 12 (37.5%) of the patients were in the primary and below primary categories respectively. Only 1 (3.1%) patient was found to be a graduate. Concerning occupation, majority were housewives, i.e., 9 (28.1) followed by unemployed 8 (25.0%). Some of the patients, meaning 6 (18.8%) were found to be farmers. With context to clinical presentation, mostly nodal presentation was seen, which was 20 (62.5%). The LDH level was reported to be normal in majority of the participants, meaning 23 (71.9%). Lastly, regarding histological classification of the tumor, most frequently occurring tumors were either B cell type or NOS (not otherwise specified) type, being 12 (37.5%) or 11 (34.4%), respectively [Table 1].

The figure demonstrates the clinical features or symptoms of the patients. Majority of the patients, were 18 (56.3%) presented with neck swelling. The next common presenting symptoms were B symptoms, which were found in 11 (34.4%) patients [Figure 1].

The figure explains about the staging of the NHL in the patients as per the AAS classification. Majority of the patients was 15 (46.9%) belonged to Stage II followed by 9 (28.1%) patients in Stage III [Figure 2].

In concern to the sites of involvement, the majority of the patients had cervical nodal involvement, which is 13 (40.6%); followed by supra clavicular lymph nodes, i.e., 7 (21.9%). Regarding number of sites, most of the patients had 1-3 sites involved, which was 18 (56.3%), followed by 4-6 lymph nodes that is 9 (28.1%) patients of NHL [Table 2].

It was noted that among the total 32 patients of NHL, 23 of them were reported to have developed extranodal involvement. Regarding sites, commonest to be found were the gastrointestinal tract followed by the lungs, which were 7 (21.9%) and 5 (15.6%) out of the 23 patients respectively. Renal and adrenal involvement was relatively uncommon. Concerning number of sites, most of the cases were of single extranodal presentation, meaning 17 (53.1%) [Table 3].

It was seen that, 19 (59.4%) of the cases fell into DLBCL category of tumors followed by 8 (25.0%) which were in the follicular lymphoma category. T cell lymphoma was rare; only 2 (6.2%) cases were found. [Figure 3].

Table 1: Socio-demographic and clinical presentation of the patients (n=32)

Patient profile	Frequency (%)
Age (in years)	
≤20	4 (12.5)
21-40	8 (25.0)
41-60	10 (31.3)
>60	10 (31.3)
Range	17-75
Gender	
Male	22 (68.8)
Female	10 (31.3)
Ratio (male: female)	2.2:1
Educational status	
Illiterate	3 (9.4)
Below primary	12 (37.5)
Primary	13 (40.6)
Secondary	3 (9.4)
Graduate	1 (3.1)

Occupation	
Housewife	9 (28.1)
Unemployed	8 (25.0)
Farmer	6 (18.8)
Service holder	5 (15.6)
Student	3 (9.4)
Electrician	1 (3.1)
Performance status (ECOG)	
0	14 (43.7)
1	8 (25.0)
2	5 (15.6)
3	3 (9.3)
4	2 (6.2)
Clinical presentation	
Nodal	20 (62.5)
Extranodal	12 (37.5)
Levels of LDH	
Normal	23 (71.9)
Raised (>ULN)	9 (28.1)
Histological characteristics of the tumor	
B cell type	12 (37.5)
NOS	11 (34.4)
Germinal cell type	7 (21.9)
T cell type	2 (6.3)

*ECOG: European cooperative oncology group performance scale; LDH: Lactate dehydrogenase; ULN: Upper limit of normal; NOS: Not otherwise specified.

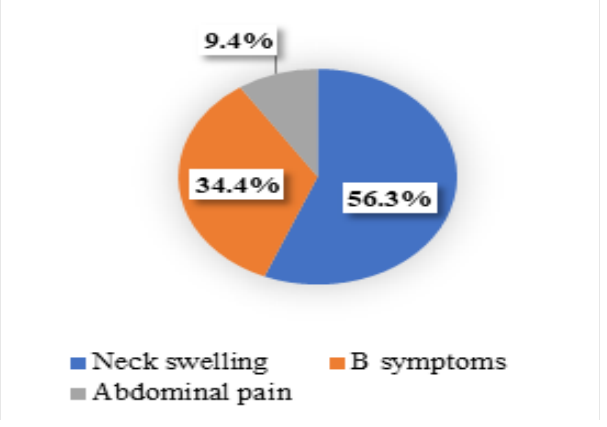


Figure 1: Symptoms of the participants (n=32)

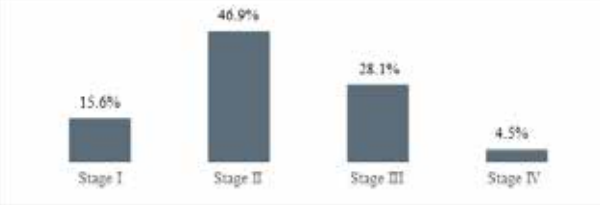


Figure 2: Staging of the tumor according to Ann Arbor staging classification (n=32)

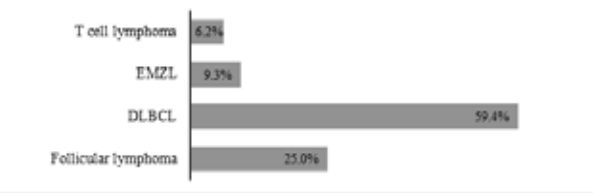
Table 2: Nodal sites on primary presentation (n=32)

Nodal involvement	Frequency (%)
Sites of nodal lymphadenopathy	
Cervical	13 (40.6)
Supra clavicular	7 (21.9)
Inguinal	5 (15.6)
Axillary	2 (6.3)
Mesenteric	2 (6.3)
Retroperitoneal	2 (6.3)
Para aortic	1 (3.1)
Number of sites of nodal involvement	
1-3	18 (56.3)
4-6	9 (28.1)
>6	5 (15.6)

Table 3: Extranodal sites on primary presentation (n=23)

Extranodal involvement	Frequency (%)
Sites of extranodal involvement	
GIT	7 (21.9)
Lungs	5 (15.6)
Liver	4 (12.5)
Head and neck	3 (9.4)
Skin	2 (6.3)
Renal	1 (3.1)
Adrenal	1 (3.1)
Number of site of extranodal involvement	
Single	17 (53.1)
Multifocal	6 (18.8)

*9 respondents had no extranodal involvement that is why n=23; GIT: Gastrointestinal tract.



*DLBLC: Diffuse large B cell lymphoma; EMZL: Extra-nodal marginal zone lymphoma.

Figure 3: Impression of tumors on the basis of immunohistochemistry (n=32)

Discussion

A total of 32 patients were recruited for this study. We found that the most common age groups were 41-60 years and over 60 years, with an age range of 17 to 75 years. The majority of participants were male, resulting in a male-to-female ratio of 2.2:1. Most had an educational level up to primary or below primary, and many were

housewives or unemployed. The ECOG performance status was predominantly 0, and clinical presentations were frequently nodal. LDH levels were mostly within normal ranges, and B-cell type and not otherwise specified (NOS) tumors were the most commonly reported. In a previous study conducted in Mangalore, India, the age range was 9 to 76 years, with a male-to-female ratio of 2:1.[10] Another study from a regional cancer center in Northeast India in 2017 reported an age range of 9 to 84 years and a male-to-female ratio of 1.2:1. Regarding ECOG status, a score of 0 was common, occurring in 42% of cases, and 57% of participants reported nodal presentation as the primary clinical feature. LDH levels were equally split, with 50% of cases reporting normal levels and 50% showing elevated levels. Lastly, B-cell type was the most frequently encountered tumor based on immunophenotyping.[11] Certain differences can be attributed to lifestyle patterns and overall variations across countries.

Neck swelling and B symptoms were identified as the most common presenting features among the patients. A similar study reported that neck swelling and B symptoms were observed in 58% and 47% of cases, respectively.[11] Another study found that abdominal pain was prevalent in 55.1% of respondents, compared to 36.7% experiencing B symptoms. In this case, neck swelling was the predominant finding, occurring in 61.2% of patients.[12] Notably, B symptoms were a group of symptoms that include fever, drenching night sweats, and a loss of more than 10% body weight in the previous six months.[13]

Furthermore, based on AAS, we found that 46.9% of patients were classified as Stage II, with 28.1% falling into Stage III. Another study conducted in Bangladesh found that the most frequently seen stages were I and II (46.2% and 42.3%, respectively).[14] The difference could be explained by other tumor-related factors.

In terms of nodal involvement at initial presentation, cervical lymphadenopathy was the most prevalent finding, affecting 40.6% of patients. The next most common sites were supraclavicular and inguinal lymphadenopathies. Additionally, 56.3% of patients had 1 to 3 lymph nodes involved. A previous study reported that 65% of patients had cervical lymphadenopathy, followed by inguinal and axillary lymphadenopathy, with 31% having 1 to 3 lymph nodes affected.[11]

In context of extranodal involvement, 23 patients out of 32 had these features. Among them, gastrointestinal tract and lung lymph node involvement was most often seen; 21.9% and 15.6% respectively. Furthermore, more than 50% patients had a single extranodal site involved. In a Bangladeshi study, only 27% patients exhibited extranodal involvement.[14] Another study said that, 17% and 14% patients had gastrointestinal and head and neck lymph nodal involvements respectively.[11]

59.4% of patients were classified as having diffuse large B-cell lymphoma (DLBCL), while 25% fell into the follicular lymphoma category based on immunohistochemistry. A study conducted in India reported similar findings, noting that DLBCL was the most common type, accounting for 34% of all NHLs.[15] Another study conducted in Saudi Arabia indicated that 59% of the cases were DLBCL.[16]

Conclusion

Non-Hodgkin's lymphoma is characterized by a diverse clinical presentation and pathological profile. In summary, our most significant findings included patients over 40 years old, predominantly male, with nodal presentations, histologically confirmed B-cell types, and diffuse large B-cell lymphoma (DLBCL) identified through immunohistochemistry. Common symptoms included neck swelling, and Stage II tumors often exhibited both nodal and extranodal involvement, particularly in the cervical region and gastrointestinal tract, respectively. There is a need for comprehensive research on a larger scale regarding the manifestations and management of NHL, which could facilitate early diagnosis and prompt treatment of this potentially curable disease.

Acknowledgements: We thank the study team and participants for their contribution of the study. We also thank the hospital authorities for their kind cooperation.

Conflict of interest: The all authors declared no conflict of interest.

Financial support: This study didn't receive any funding.

References

1. Singh R, Shaik S, Negi BS, Rajguru JP, Patil PB, Parihar AS, Sharma U. Non-Hodgkin's lymphoma: A review. Journal of family medicine and primary care. 2020;9(4):1834-40.
2. Thandra KC, Barsouk A, Saginala K, Padala SA, Barsouk A, Rawla P. Epidemiology of non-Hodgkin's lymphoma. Medical Sciences. 202;9(1):5.
3. Fisher SG, Fisher RI. The epidemiology of non-Hodgkin's lymphoma. Oncogene. 2004;23(38):6524-34.
4. Shafer WG, Hine MK, Levy BM, Rajendran R, Sivapathasundharam B. Shafer's textbook of oral pathology. Diseases of the Skin. Rajendran R, editor. 2006; 5:1103-7.
5. Feugier P, Filliatre-Clement L. Recent advances in the first-line treatment of follicular non-Hodgkin lymphoma. F1000Research. 2019;8.
6. Armitage JO. Staging non-Hodgkin

lymphoma. CA: a cancer journal for clinicians. 2005;55(6):368-76.

7. Kesavan M, Eyre TA, Collins GP. Front-line treatment of high-grade B cell non-Hodgkin lymphoma. Current Hematologic Malignancy Reports. 2019; 14:207-18.
8. Ansell SM, Armitage J. Non-Hodgkin lymphoma: diagnosis and treatment. Elsevier. 2005;80(8):1087-1097
9. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, Carbone PP. Toxicity and response criteria of the Eastern Cooperative Oncology Group. American journal of clinical oncology. 1982;5(6):649-56.
10. Impana BD, Teerthanath S, Sunil Kumar Y, Kishan Prasad HL, Jayaprakash Shetty K. Clinicopathological Study of Malignant Lymphomas. Journal of Dental and Medical Sciences. 2016;15(10):82-.
11. Devi AA, Sharma TD, Singh YI, Sonia H. Clinicopathological profile of patients with non-hodgkin's lymphoma at a regional cancer center in Northeast India. Journal of the Scientific Society. 2017;44(3):140-4.
12. Hingorjo MR, Syed S. Presentation, staging and diagnosis of lymphoma: a clinical perspective. J Ayub Med Coll Abbottabad. 2008;20(4):100-3.
13. Mugnaini EN, Ghosh N. Lymphoma. Primary Care: Clinics in Office Practice. 2016 Dec 1;43(4):661-75.
14. Ahmed T, Begum F, Begum SM. Value of PET-CT Staging in Lymphoma Patients at Baseline over Clinical Staging. Bangladesh Journal of Nuclear Medicine. 2019;22(1):15-22.
15. Naresh KN, Srinivas V, Soman CS. Distribution of various subtypes of non-Hodgkin's lymphoma in India: a study of 2773 lymphomas using REAL and WHO Classifications. Annals of oncology. 2000;11:S63-7.
16. Alyahya N, Adiga B, Alwadei A, Alshahrani G, Alyahya F. The clinico-pathological profile of non-Hodgkin's lymphoma in Aseer region of Saudi Arabia. BMC Research Notes. 2019;12:1-7.