



HISTOMORPHOLOGICAL SPECTRUM OF MALIGNANT LYMPHOMA IN TERTIARY CARE CENTRE IN HADOTI REGION

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ABSTRACT

BACKGROUND: In hadoti region, we had analyzed all malignant lymphomas with aspect of age, sex, site, clinical features and type according to WHO classifications. This study aims to analyze histomorphological spectrum of lymphomas in a tertiary care center in hadoti region. **MATERIAL AND METHODS:** 56 Lymphoid neoplasms of all age group diagnosed within 5 years from January 2012 to December 2016 in tertiary care centre, hadoti region, were analyzed. Clinical history, physical examination and available laboratory investigation were evaluated. The final diagnosis was based on histology according to WHO classification 2008 and four cases were confirmed with immunohistochemistry. **RESULTS:** Out of 56 cases of lymphoma, 66.1% (37 cases) were diagnosed as Non-Hodgkin lymphoma and 33.9% (19 cases) as Hodgkin disease, with an overall male predominance. Lymphadenopathy was the commonest presenting features in both the types of Lymphomas. On histopathology, majority of Non-Hodgkin lymphomas, 13 cases (35.13%) showed a diffuse pattern, while nodular sclerosis was the commonest type seen in Hodgkin disease 7 cases (36.8%). **CONCLUSION:** Non-Hodgkin lymphomas are two times more common than Hodgkin lymphoma. Patient presenting with lymphadenopathy with systemic features of lymphoma should be concerned and full work up should be done with presenting symptoms, physical examination, complete laboratory investigation and histopathological examination.

KEYWORDS

Non-Hodgkin lymphoma and Hodgkin lymphoma

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INTRODUCTION

Lymphomas are malignant disorders of cells residing in lymphoid tissues and are classified into two main types; Hodgkin disease (HD), and Non-Hodgkin lymphoma (NHL). Lymphoma can occur at any age; however, it has a bimodal presentation with one peak in early years of life and other after middle age. The diagnosis of lymphoma involves histopathological findings on biopsy of an enlarged lymph node from a relevant site, aided further by invasive or non-invasive procedures to confirm the extent of disease, and to formulate a proper therapeutic plan. Lymphomas are treatable and frequently curable malignancies. The WHO classification of lymphoid neoplasm includes Hodgkin lymphoma and non-Hodgkin lymphoma (NHL) as well as plasma cell neoplasm and lymphoid leukemia, with theory that lymphoma and lymphoid leukemia represent solid and circulating phases, respectively, of the same disease.[1-3]

Clinically, NHL is divided into, low grade, intermediate grade, and high grade lymphomas. The Ann Arbor staging system is the most popular system for classifying lymphomas into different stages.[4]

Lymphoid neoplasms are the sixth most common malignancy worldwide. Malignant lymphoma comprises 3.37% of all malignancy worldwide.[5] Geographic variation in lymphoma rate suggests the importance of environmental and genes effects.[6]

The present study was undertaken to subtype the malignant lymphoma in this part of the world according to WHO classification and to know histomorphological spectrum of malignant lymphoma.

PATIENTS AND METHODS

In our retrospective study, 56 diagnosed cases of lymphoma were selected from Government Medical College, Kota and associated hospitals from 2012 to 2016. Patient's data regarding clinical history, physical examination, laboratory investigations and diagnosis were

retrieved from hospital records. Patients presenting with symptoms of lymphadenopathy and other systemic organ involvement were examined and biopsy of the affected lymph node or the organ was taken by the surgeons, after receiving an informed consent from the patient. The histopathological examination of lymph node and/or other involved organ was done and diagnosis was made.

Inclusion criteria: The study included patients of all age group

Exclusion criteria: patients having chronic lymphocytic leukemia, plasma cell myeloma, precursor B and T lymphoblastic leukemia.

The diagnosis of lymphoma was based on histology according to the WHO 2008 classification.

PROCEDURE:

All the biopsy specimens of enlarged lymph node and extranodal sites of lymphomas, which were sent to the department of Pathology, Government medical college, Kota were included in the study.

Biopsy and excision specimens were fixed in 10% formalin and then processed. Section of 4 micrometer were mounted on glass slide and stained with hematoxylin and eosin (H&E) stain. Special stains as reticulin stain and PAS stain were done wherever necessary. Immunohistochemistry was done in four cases only.

RESULTS

TABLE 1: Incidence of Hodgkin and Non Hodgkin lymphoma according to age

Age (years)	HL	NHL	Total
0-10	2	2	4
11-20	1	2	3
21-30	4	6	10

31-40	5	5	10
41-50	3	6	9
51-60	2	7	9
61-70	2	6	8
71-80	0	3	3
Total	19	37	56
Mean age	36.7	45	

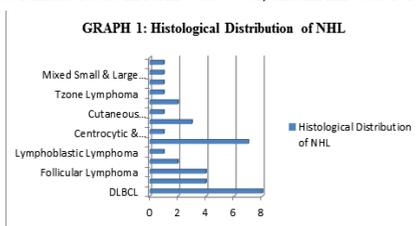
56 cases of malignant lymphomas were studied. NHL comprised of 66.1% (37 cases), while HL comprised of 33.9% (19 cases).

TABLE 2: Incidence of Hodgkin and Non-Hodgkin lymphoma according to sex

	HL	NHL	Total
Male	10	29	39
Female	9	8	17
	19	37	

Majority of the patients were males (39 cases), with a male to female ratio of 2.3:1.

The male to female ratio in NHL was 3.6:1, and in HL was 1.1:1

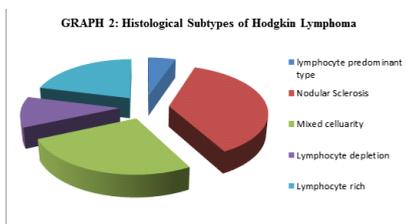


Among NHL, DLBCL was the most common histological subtype accounting 21.6% followed by 18.9% of Diffuse NHL

TABLE 3: Distribution of Nodal and extranodal site of involvement by lymphoma

Type of lymphoma	Total
Nodal	37(66.1%)
Extra nodal	19(33.9%)
1. Intestine	6
a) Stomach	1
b) Ileocaecal	3
c) Colon	1
d) Rectum	1
2. Testies	1
3. Soft tissue	6
4. CNS	1
5. Bone	1
6. Liver	1
7. Weldeyers ring	1
8. Oral cavity	1
9. Nasal cavity	1

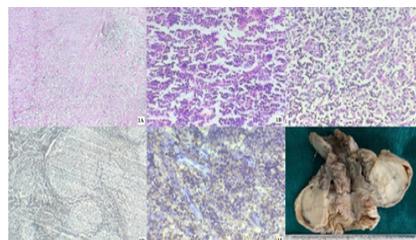
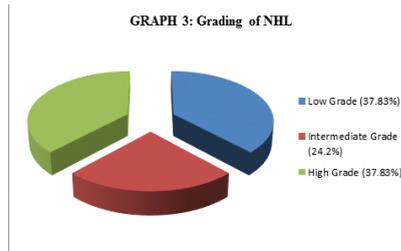
Both nodal and extranodal lymphomas accounted for 66.1% and 33.9% respectively. Most common site of extranodal lymphoma was gastrointestinal tract (31.57%), and soft tissue (31.57%).



In HL, nodular sclerosis HL (36.84%) was the most common type encountered followed by mixed cellularity (26.31%) then lymphocyte rich (21.05%).

Childhood lymphomas was encountered in 4 cases, of which two case

were of Hodgkin lymphoma, one was lymphoblastic lymphoma and one was of DLBCL.



MICROPHOTOGRAPHS

1A: Hodgkin Lymphoma – Nodular Sclerosis type showing lymphoid tissue separated by dense bands of collagen (H&E stain, 400X).

1B: Section of Hodgkin Lymphoma – Nodular Sclerosis type showing monolobated Reed Sternberg cells (H&E stain, 400X).

1C: Section of Diffuse Large B Cell Lymphoma showing diffuse proliferation of large pleomorphic neoplastic B lymphoid cells (H&E stain, 400X).

1D: Section of Follicular Lymphoma showing variable sized follicles well demarcated by reticulin fibres (Reticulin Stain, 400X).

1E: Immunohistochemistry CD 20, Section showing diffuse positivity of tumor B cells (400X).

1F: Gross photograph of intestine showing large homogenous grey white well defined tan colored mass.

DISCUSSION

In the present study, 56 cases of malignant lymphomas were analyzed.

NHL was the most common type of lymphoma accounting for 66.1% of cases and HL was seen in 33.9% of cases. This is in concordance with study conducted by Claude et al (2014)[7] which was 24% and 76% respectively and in various studies conducted by Mozaffer et al (2008)[8], Yang et al (2011)[9], and Waravita et al (2015)[10] there is increased differences between HL and NHL.

In our study, mean age in NHL and HL was 45 and 36.7 years respectively, which was comparable with Yaqo R T et al 2011(45 year)[11] and T S Waravita et al 2015[10] (49.83 year) in respect of NHL and comparable with Santosh Kumar Mondal et al 2013[12] (31.3 year) in respect of HL.

NHL was more commonly seen in elderly population predominantly than in younger adults. Thus, age presents to be a strong risk factor in NHL.[13]

In the study group, malignant lymphomas were more common in male (69.6%) with a male to female ratio of 2.3:1. Both NHL and HL showed a male preponderance which was in agreement with studies by Yakubu M et al (2015)[14], 2.6:1 ratio and Mondal S K et al (2013)[12], 3.1:1 ratio and BD Impana et al (2016) [13] ratio was 1.9:1

Malignant Lymphoma can present with nodal or extranodal manifestations. Majority of the cases of NHL showed extranodal involvement (45.9%), whereas only 2 cases of HL were of extranodal type. This was similar to studies by BD Impana et al (2016)[13], Jin man et al (2011)[15] and Sun et al (2012)[16], who also observed higher incidence of extranodal lymphomas among NHL. However Mondal et al (2013)[12] found a higher incidence of nodal type of NHL.

In nodal lymphomas of NHL, cervical group of lymph nodes were most commonly involved, followed by axillary and inguinal lymph nodes. This was in concordance with studies by Impana et al 2016 [13], Santosh et al (2013)[12] and Sudipta et al (2010)[17].

In HL, the most common lymph node involved was cervical group followed by axillary, supraclavicular, submandibular and thoracic group of lymph nodes, which was similar with the study done by Impana et al 2016[13] and Sudipta et al (2010).[17]

The frequency of extranodal NHL varies in different parts of the world. Gastrointestinal tract and soft tissue were the most common site and was involved in 31.5% of all extranodal NHL each. Other studies like B D Impana et al 2016[13], Yaqo et al (2011) [11], JinMan et al (2011)[15], Sun et al (2012)[16] and Mondal et al (2013)[12] also encountered gastrointestinal tract as the most common site of NHL.

The most common type of lymphoma in extranodal site was NHL NOS which was not in concordance with many studies as Yang et al (2011)[9] and Waravita et al (2015).[10]

The most common histological subtype of NHL encountered in our study is DLBCL (21.6%) followed by diffuse NHL-NOS type (18.9%), MALToma and Follicular lymphoma (10.8%) each. This was in comparison with other studies by Wei et al (2011)[18], Jin-Man et al (2010)[15], Sun et al (2012)[16] and Santosh Kumar Mondal et al (2013).[12]

Follicular lymphoma occurs more frequently in India.

Naresh et al proposed that, in developing countries, the low rates of Follicular Lymphoma compared to DLBCL may be due to progression of previously undiagnosed Follicular Lymphoma.[19]

Our study excluded plasma cell neoplasm so these results may not be comparable with population-based incidence data for the entire spectrum of WHO classification. Both REAL and WHO classification encompass not only Hodgkin lymphoma and non-Hodgkin lymphoma but also plasma cell neoplasm and lymphoid leukemia, which represent solid and circulating phases of the same disease.

Two cases of CLL/SLL were encountered in our study. According to Waravita et al [10], the prevalence of CLL/SLL remains low in south and east Asian countries highlighting that genetic bias and host related genetic factors play a role in the pathogenesis.

Grading of NHL was done according to working formulation classification. Dividing the lymphomas into low, intermediate, and high-grade categories helps in the management of the patients and has prognostic implications. In our study, 37.83% of NHL were classified as high grade, 37.83% as low grade followed by 24.32% as intermediate grade.

The most frequent histological subtype of HL in the current study is nodular Sclerosis (36.84%) followed by mixed cellularity (26.3%). This was in concordance with other studies like Yaqo et al (2018)[11] distribution was 48% and 37% respectively. Jin man et al (2011) [15] also found a higher incidence of nodular sclerosis type of CHL (47.4%) compared to MCCHL (30.6%).

Immunohistochemistry was done on 4 cases only of malignant lymphomas in our study. Various antibodies used were of Pan B-cell markers were CD 20, CD45, BCL 2, cyclin D1 and Pan T-cell markers included CD 3, CD 30 with LCA and Ki-67. Our study showed two cases of mixed cellularity of Hodgkin lymphoma, one case of follicular lymphoma and one case of DLBCL on the basis of IHC.

The therapeutic strategies are guided by the clinical features and histological findings.

CONCLUSION

Our study shows twice the number of NHL cases (66.1%) than HL cases (33.9%) and male–female ratio is 2.3:1. NHL is more commonly seen in the old age. The most common sub types of NHL is diffuse large B cell lymphoma followed by diffuse NHL NOS type.

Among HL, Nodular Sclerosis HL was predominant type than Mixed Cellularity HL, which is similar to the trend in some other Middle East

countries and approaching the pattern seen in western countries; however, unlike other Asian and Indian studies where mixed cellularity is the commonest type.

There is increase in the incidence of lymphomas in India and worldwide. The distribution of NHL subtypes in India shows important differences with those from the rest of the world. There is a rise in the incidence of extranodal primary lymphoma with involvement of gastrointestinal tract and soft tissue predominantly.

Grading and staging of lymphomas has therapeutic and prognostic implications. Immunohistochemistry is a useful and necessary diagnostic aid and helps in sub-typing different types of NHL.

A general awareness regarding the clinical manifestations of lymphomas, along with usage of advanced investigative techniques may lead to early diagnosis and proper management of the disease.

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