

## Original Research Article

# Clinico-pathological analysis of lymphoproliferative disorders: a 3 year study

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## ABSTRACT

**Background:** The incidence of lymphoproliferative disorders has increased in many parts of the world. Newer subtypes have been identified by the new WHO classification. Accurate subtyping of lymphomas is crucial for prompt treatment. Objective of the study was to assess the clinicopathological pattern of lymphoproliferative diseases diagnosed in Rajagiri hospital over a period of 3 years.

**Methods:** A retrospective study on all patients who were diagnosed with lymphoma in Rajagiri hospital during January 2016 to December 2018 was conducted and the data were reviewed and analyzed.

**Results:** A total of 151 patients were included in the study. Majority of the subjects (63%) were males. The predominant age group affected was 61-80 years. Mean age group was 58.46 years (SD=19.05 years). Most common presenting symptom was painless lymphadenopathy. B symptoms were seen in 18% of subjects and was found to be more commonly associated with B cell Non-Hodgkin lymphoma. Most common lymph node involved was cervical lymph node, while the most common extra nodal site was bone marrow. Most common lymphoproliferative disorder was Diffuse large B cell Lymphoma. Lymph node involvement was found in 74% of patients, while hepatomegaly and splenomegaly were seen in 11% and 18.5% of patients. 20% of patients had secondary bone marrow involvement. 8 patients developed recurrent lesions involving other organs.

**Conclusions:** Clinicopathologic patterns of lymphoproliferative disorders vary across various regions. A proper understanding of demographical distribution of lymphomas is very essential, as it can provide valuable clues for accurate diagnosis and treatment.

**Keywords:** Bone marrow involvement, Cervical lymphadenopathy, Diffuse large B cell lymphoma, Follicular lymphoma, Peripheral T cell lymphoma, Splenomegaly

## INTRODUCTION

Lymphoproliferative disorders are a heterogenous group of neoplasms of lymphoid cells, including B, T or NK cells. The incidence of these neoplasms has shown a rising trend in many countries. Lymphomas account for 3% of all malignancies. The age adjusted incidence rate of Non-Hodgkin lymphoma among men and women in India are 2.9/ 1,00,000 and 1.5/1,00,000 respectively.<sup>1</sup>

There are geographic variations in the distribution of lymphomas. The lympho-proliferative disorders are broadly divided into Hodgkin lymphoma and Non-Hodgkin lymphomas, based on morphology and immunophenotypic features.

Recent advances in immunohistochemical markers and molecular methods aid in accurate subtyping, which carries grave prognostic significance. This study aims to

assess the recent trends in clinicopathological patterns of lymphoproliferative disorders over a period of 3 years. Objective of the study was to assess the clinicopathological pattern of lymphoproliferative diseases diagnosed in Rajagiri hospital over a period of 3 years.

**METHODS**

The study was a retrospective and cross-sectional study conducted in the Department of pathology, Rajagiri Hospital. The study subjects included all the patients who were diagnosed with lymphoma in Rajagiri Hospital from the time period January 2016 to December 2018.

**Exclusion criteria**

- The recurrent lesions.

Relevant clinical information was obtained from the electronic case records of the patient. Clinical details that were collected include age, gender, presenting symptoms and duration, site of tumor, and assessment of involvement of lymph nodes, liver, spleen or other organs. The complete blood counts, including hemoglobin, total count and platelet count, at the time of diagnosis was studied. Paraffin embedded blocks, H and E stained slides and Immunohistochemistry slides of the patients available in the Department of Pathology were studied for pathological sub-typing of lymphoma and assessment of bone marrow involvement. The data was entered in the spreadsheets of Microsoft Office Excel and the variables were analyzed using standard analytic techniques with SPSS version 16.0 for Windows. The quantitative variables were expressed as mean and qualitative variables were expressed as percentages.

**RESULTS**

A total number of 151 subjects were included in the study. It included 95 males (63%) and 56 females (37%). Most subjects belonged to the age group 61-80 years, ranging from 4-100 years. Mean age was 58.46 years (SD=19.05). Most common presenting symptom was painless swelling (21%) followed by B symptoms (18%). B symptoms were noted in 27 subjects.

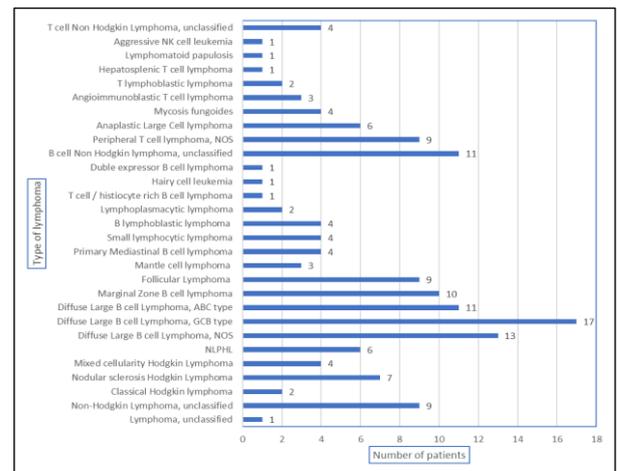
B symptoms were found to be most commonly associated with B cell Non-Hodgkin Lymphomas (44%) followed by T cell Non-Hodgkin Lymphomas (26%) and Hodgkin lymphomas (22%). 80 patients (53%) had nodal disease at the time of presentation. Most commonly affected lymph node was cervical lymph node (40%) followed by inguinal lymph node (21%). Predominant extra nodal sites of involvement were bone marrow (35%) followed by skin (8%), mediastinum (6%) and nasopharynx (7%). The nodal and extra-nodal sites at initial presentation are described respectively in in tables 1 and 2.

**Table 1: Distribution of nodal lymphoproliferative diseases.**

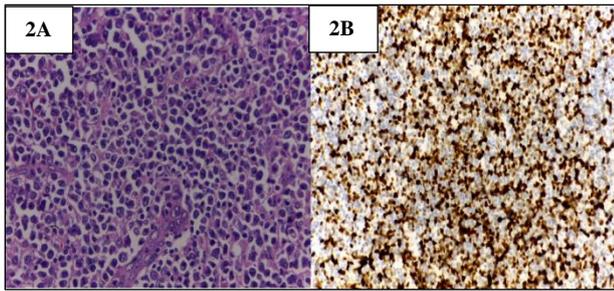
Lymph node affected	Number
Cervical node	32
Inguinal node	17
Axillary node	9
Retroperitoneal node	6
Mesenteric node	4
Supraclavicular node	4
Iliac node	3
Portocaval and hepatic node	5

**Table 2: Sites of extra nodal lymphoproliferative diseases.**

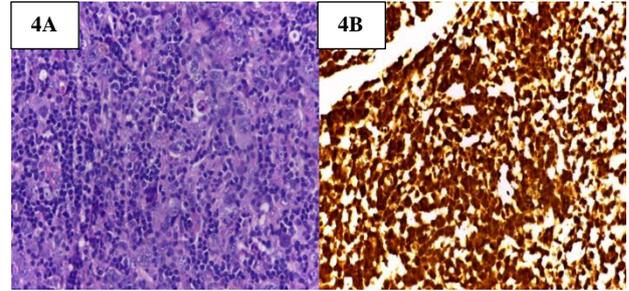
Extra-nodal site	Number
Head and neck	
Nose and nasopharynx	5
Brain	3
Tonsil	1
Tongue	1
Orbit	1
Gastrointestinal tract	
Esophagus	1
Stomach	3
Small intestine	3
Colon	1
Liver	1
Intra-abdominal mass	1
Peritoneum	1
Pelvic mass	1
Vertebra	1
Rib	1
Bone marrow	25
Skin	6
Breast	3
Testis	2
Mediastinum	5
Chest wall	3



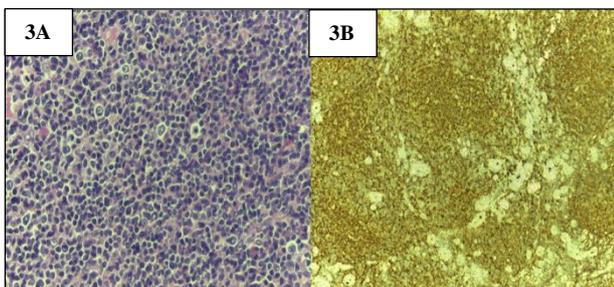
**Figure 1: Distribution of subtypes of lymphoproliferative diseases.**



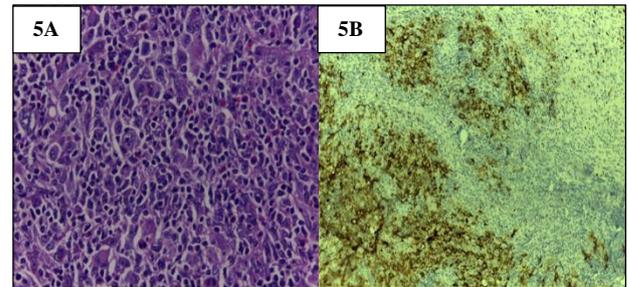
**Figure 2: A) (400x)- Diffuse Large B Cell Lymphoma- shows large atypical cells with moderate cytoplasm, enlarged nuclei and prominent nucleoli, B) (100x)- Diffuse Large B Cell Lymphoma - shows high Ki67 index.**



**Figure 4: A) (400X) Anaplastic Large cell lymphoma- shows large atypical cells admixed with eosinophils, lymphocytes and plasma cells, B) (400X) Anaplastic Large cell lymphoma- Tumor cells are positive diffusely for ALK.**



**Figure 3: A) (400 X)- Follicular lymphoma- Shows a tumor composed of small cleaved cells and non-cleaved cells with multiple nucleoli, B) (100X) - Follicular lymphoma- Tumor shows strong diffuse positivity for CD10.**



**Figure 5: A) (400x) Hodgkin Lymphoma, Mixed Cellularity subtype- Shows mononucleated Hodgkin cells admixed with eosinophils and plasma cells, B) (100x) Hodgkin cells show membranous positivity for CD15.**

**Table 3: Age and sex distribution of the subtypes of lymphoproliferative disease.**

Age	Sex	Lymphoma	Non-Hodgkin lymphoma			Hodgkin lymphoma	
			Unclassified	B cell	T cell	CHL	NLPHL
0-20 years	Male		3		1	1	1
	Female			2		1	
21-40 years	Male			2	3	4	1
	Female			3	2	2	
41-60 years	Male	1	1	17	7	2	1
	Female		2	11	3	2	2
61-80 years	Male	1	3	32	6	1	1
	Female			16	7		
81-100 years	Male			6	2		
	Female			3			

Among 139 patients whose laboratory values were available, 66 had anaemia (47%), 17 had leukopenia (12%), 22 had leukocytosis (15%), 26 had thrombocytopenia (19%) and 9 had thrombocytosis (6%) at the time of diagnosis. Among 25 subjects with bone marrow involvement at the time of presentation, 22 (88%) had abnormal blood parameter. The distribution of

different subtypes of lymphoproliferative disorders were assessed and is depicted in Figure 1. Most common type of lymphoproliferative disorder was B cell Non-Hodgkin Lymphoma (60%), followed by T cell Non-Hodgkin lymphoma (20.5%). Diffuse Large B Cell Lymphomas (Figure 2 A and B) were the most common subtype, followed by Marginal zone B cell lymphoma, Follicular

lymphoma (Figure 3 A and B) and Peripheral T cell lymphoma. 2 patients with follicular lymphoma also had an associated Diffuse large B cell lymphoma component. Other lymphomas noted were Anaplastic large cell lymphoma (Figure 4 A and B), and Hodgkin lymphoma (Figure 5 A and B). The age and sex distribution of the lymphomas are summarised in Table 3. Organ

involvement in different subtypes are described in Table 4. Lymph node involvement was seen in 103 (74%) patients, hepatomegaly was seen in 16 (11%) patients and splenomegaly in 28 (18.5%) patients. 25 subjects had secondary bone marrow involvement. 8 patients developed recurrent lesions involving other organs.

**Table 4: Organ involvement in subtypes of lymphoproliferative disease.**

Organ involvement	Lymphoma	Non-Hodgkin lymphoma			Hodgkin lymphoma		
		B cell NHL	T cell NHL	Unclassified	Classical HL	NLPHL	
Lymph node	Present	1	59	23	3	11	6
	Absent		30	3	5	1	
Liver	Present		9	4		2	1
	Absent	1	80	22	8	10	5
Spleen	Present		17	5	2	1	3
	Absent	1	72	21	6	11	3
Bone marrow	Present		16	6	2		1
	Absent	1	63	19	6	12	5

**DISCUSSION**

In this study the males were more commonly affected, with a male: female ratio of 1.7 :1. This is in concordance with study done by Nair et al, where the ratio was found to be 1.6: 1.<sup>2</sup> The most common age group affected was 61-80 years, with a mean age of 58.46 years. This corresponds to other studies which demonstrates a median age of 54 years in Asian countries.<sup>3</sup> However, a few Indian studies showed mean age group to be almost a decade earlier.<sup>4</sup>

The patients most commonly presented with a painless swelling. The most common nodal site affected was the cervical nodes followed by inguinal lymph nodes. This is in concordance to similar study in North India by Devi et al, where cervical lymphadenopathy was the most common site affected.<sup>5</sup> In this study, 18% of patients had B symptoms. This was lower than the observations in similar studies done in India.<sup>4-7</sup>

Hepatomegaly was noted in 11% of patients while splenomegaly was found in 18.5% of patients. This was lower than similar studies in India but is almost similar to results from a European study.<sup>8</sup> 53% of subjects had nodal disease at the time of presentation. This is lower than similar studies in North India by Bhatia et al, where nodal disease was present in 71.5% of patients at the time of presentation.<sup>9</sup>

In this study 47% had anemia, 12% had leucopenia, 15% had leukocytosis, 19% had thrombocytopenia and 6% had thrombocytosis at the time of presentation. In a study done by Conlan et al, anemia was present in 42%, leukopenia in 6%, thrombocytopenia in 13%,

leukocytosis in 26% and thrombocytosis in 14% at the time of presentation.<sup>10</sup> The study by Conlan et al, also highlights that bone marrow involvement by lymphomas is usually associated with abnormal hematological parameters.<sup>10</sup>

The most common extra-nodal site involved was bone marrow followed by head and neck and skin. This is in contrast to studies from south India, where head and neck was the most frequent extra-nodal site.<sup>11</sup> However, this is in concordance with a similar study done in 1999 by Aziz et al.<sup>12</sup>

B cell lymphomas accounted for 60% of all lymphoproliferative disorders. This tallies with similar studies done by Naresh<sup>13</sup> et al, where B cell lymphomas accounted for 79% of all non-Hodgkin lymphomas. The slightly lower rate in this study could be explained by the fact that this study was not limited to Non-Hodgkin lymphomas.

Most common lymphoproliferative disorder in this study was Diffuse large B cell lymphoma, which constituted 27% of all lymphomas. This was followed by marginal zone lymphoma. Many Indian studies have also demonstrated similar results with a higher percentage of Diffuse large B cell lymphoma.<sup>13,14</sup> Among the diffuse large B cell lymphomas which were subtyped further into molecular subtypes, Germinal Centre B cell type was found to be more common. This is in concordance with studies in the West.<sup>15</sup>

The most common T cell Non-Hodgkin Lymphoma in this study was Peripheral T cell Lymphoma, Not otherwise specified (PTCL, NOS). This agrees with a

similar study done by Gogia et al.<sup>16</sup> The second common was Anaplastic Large Cell Lymphoma, followed by Mycosis fungoides. 20% of subjects had secondary bone marrow involvement by lymphoma. This is in concordance with a study done in China, where 16% of subjects developed bone marrow involvement.<sup>17</sup>

## CONCLUSION

Most common age group affected was 61-80 years. Males were more commonly affected. Nodal lesions were more common than extra-nodal lesion. Most common node involved was cervical lymph node. Most common extra-nodal site involved was bone marrow. Most common lymphoproliferative disorder was found to be Diffuse large B cell lymphoma. Secondary bone marrow involvement was observed in 20% of patients.

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