



## Original Research Article

## Histopathological and immunohistochemical study of lymphnodal biopsies

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## ABSTRACT

**Introduction:** Diseases affecting lymph nodes form a wide range of spectrum, from simple infection to malignant pathology. A panel of IHC markers is decided based on morphologic differential diagnosis.

**Aims and Objectives:** To study the incidence of lymph nodal lesions with respect to age and sex and their different histopathological patterns. To use Immunohistochemistry (IHC) for sub typing of neoplastic lesions.

**Materials and Methods:** This study was done for a period of two and a half years in the Department of Pathology, from Jan 2017 to June 2019. All the specimens received were fixed in 10% formalin and routinely processed and stained with Hematoxylin and Eosin (H&E.)

**Results:** A total of 230 lymph node biopsies were studied. Age distribution varied from 3 to 83 years with female preponderance. Non – Neoplastic lesions were common comprising of 120 cases (52%) while neoplastic lesions were 110 (48%). Among non neoplastic lesions reactive lymphadenitis (23%) was common followed by tuberculous lymphadenitis (21%). In neoplastic lesions, metastatic diseases (20%) predominated. IHC was done wherever necessary for subtyping of lymphomas and also to differentiate lymphoma from carcinoma.

**Conclusion:** Lymph node biopsy with IHC plays an important role in establishing the cause for lymphadenopathy and thus aids in therapy.

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## 1. Introduction

Lymph node is one of the major anatomic components of the immune system. Because normal immune response leads to proliferation and expansion of one or more of the cellular components of lymph nodes, it leads to significant lymph node enlargement.<sup>1</sup>

Lymphadenopathy is a common clinical problem and biopsies are usually undertaken to determine the cause of nodal enlargement, which may be neoplastic or non-neoplastic.<sup>2</sup>

Lymph node lesions form a wide range of spectrum from benign reactive changes to lymphoma and metastatic deposits.<sup>3</sup>

Lymphadenopathy is either generalized or localized, Generalized lymphadenopathy is seen in a large number of

systemic illnesses while localized lymphadenopathy is more often seen with local infection or malignancy.<sup>4</sup>

First step in developing better therapies is the recognition of distinct specific disease entities by pathologists. Since there is no specific treatment for most forms of reactive lymphadenopathy, even a non-specific diagnosis is helpful, because the main aim is to exclude a malignant process and treatable causes.<sup>4</sup>

Immunohistochemistry helps in the sub typing of the lymphomas into different categories which have a therapeutic and prognostic importance.<sup>5</sup>

We aim to study the incidence with respect to age and gender along with histopathological patterns of lymph nodes received in our department over a period of two and a half years

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## 2. Materials and Methods

A total of 230 lymph nodal biopsies were received in the department of pathology from January 2017 to June 2019.

### 2.1. Inclusion criteria

Excision biopsies of lymph nodes were included in the study

### 2.2. Exclusion criteria

Cases with inconclusive diagnosis due to lack of adequate material were excluded.

All the specimens were formalin fixed, paraffin embedded and stained with H and E stains.

IHC using relevant antibodies was done according to histomorphological features wherever needed. Immunohistochemical studies were carried out with 5 $\mu$  paraffin sections. The antibodies included CD3, CD15, CD20, CD30, Leukocyte Common Antigen (LCA), Pancytokeratin and Bcl-2. The lymphomas were classified according to World Health Organisation classification of hematolymphoid malignancies 2017. All cases of non Hodgkin lymphomas were subjected to B and T cell markers for sub typing. Likewise most of the Hodgkin lymphomas were subjected to immunophenotyping using CD 45, CD 15 and CD 30. In cases of ambiguity Pancytokeratin was also used to exclude metastatic deposits.

## 3. Results

This study included a total of 230 lymph node biopsies. The age range was 3-85 years and maximum cases were seen in the 21-30 years age group.

There was slight female preponderance (52%) and male to female ratio was 1:1.1

The common site was cervical lymphadenopathy seen in 60% of cases followed by inguinal (15%), axillary (8%), supraclavicular (7%), mediastinal (3%), retroperitoneal (2%) and other sites (5%).

In the 230 lymph node biopsies analyzed, the non neoplastic lesions were common comprising 52% (120 cases) and neoplastic lesions were 48% (110 cases).

The non neoplastic lesions were common in the age group 21-30 years and among them reactive lymphadenitis was the most common accounting to 26 % (61 cases). In these 61 cases, chronic non specific lymphadenitis (18%) was common followed by follicular hyperplasia (5%) and sinus histiocytosis (3%). Granulomatous lymphadenitis was the second common non- neoplastic lesion comprising 22% (49 cases) in which tuberculosis (15%) (Figure 1 A) was the most common and others were of unknown etiology. (Table 1)

Non neoplastic lesions also included 3 cases of Kikuchi lymphadenitis (Figure 2B), 2 cases of Castleman's disease of hyaline vascular type (Figure 3C) and 1 case each of

myeloid metaplasia, a ngiomatous lymph nodal hamartoma (Figure 4 D) and lipomelanotic lymphadenopathy. (Table 1)

In the 110 neoplastic lesions, metastatic diseases were common accounting to 20% (47 cases) followed by 19% (44 cases) of Non Hodgkin lymphomas and 9% (19 cases) of Hodgkin lymphomas. (Table 2).

In these neoplastic lesions 12 cases had a differential diagnosis of lymphoma/ metastatic lesion on histopathology which were later confirmed with the aid of Immunohistochemical markers CD 45 and Pancytokeratin, of which 5 cases were diagnosed as poorly differentiated adenocarcinoma and 7 cases were non Hodgkin lymphoma.

Metastatic lesions were common in the age group 61-70 years and there was a female preponderance. Among them Squamous cell carcinoma (20 cases) (Figure 2A) was the most common diagnosis followed by 13 cases of Papillary carcinoma of thyroid (Figure 2B), 9 cases of Adenocarcinoma (Figure 2C), 2 cases of Mucinous adenocarcinoma (Figure 2E) and 1 case each of Renal cell carcinoma (Figure 2D), Medullary carcinoma of thyroid (Figure 2 F) and Melanoma.

In the 44 cases of non Hodgkin lymphoma, 39 cases were of diffuse large cell lymphoma (Figure 3A), 2 cases were follicular lymphoma (Figure 4A) and 1 case each of small cell lymphocytic lymphoma (Figure 3B), anaplastic large cell lymphoma and T cell lymphoma (Figure 4C). Non Hodgkin lymphomas were common in the 41-50 years age group with an age range of 10 to 85 years. Immunohistochemistry was done in 40 cases in which 35 cases were positive for CD 20 (Figure 3C) and negative for CD 3 (Figure 3D). 2 cases were positive for BCL2 (Figure 4 B) and 2 cases were positive for CD 3 (Figure 4D). The remaining 4 cases were reported as diffuse large B cell lymphoma and IHC was not done for these cases due to economic constraint.

Hodgkin lymphomas include 19 cases, 18 cases were of classical type and 1 case was lymphocyte predominant type. In classical type of Hodgkin lymphoma, 15 cases were of mixed cellularity sub type (Figure 5A), 2 cases of nodular sclerosis sub type (Figure 5B) & 1 case of lymphocytic depletion. They were seen in age group 51-60 years. These 18 cases of classical Hodgkin lymphoma were confirmed by positivity for CD15 and CD30 as shown in (Figure 5 C&D)

## Discussion

This study included a total of 230 lymph nodal biopsies with different histopathological patterns and Immunohistochemistry was done in lymphomas for confirmation and also to differentiate lymphoma from carcinoma.

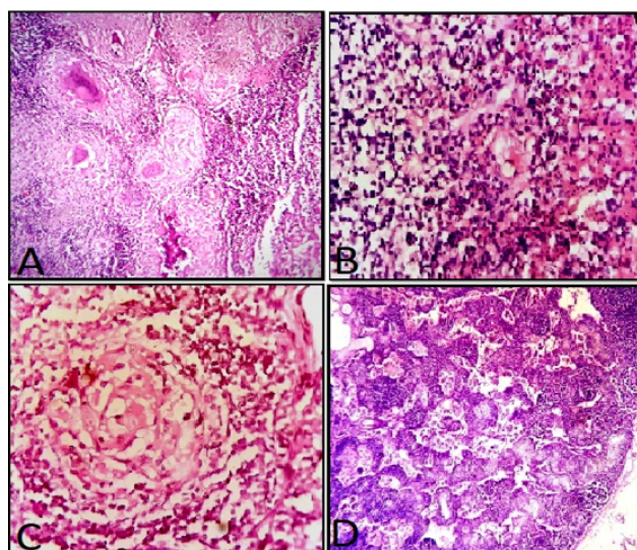
In our study maximum number of cases were seen in the age group of 21-30 years which was similar to a study done by Rajashri P et al<sup>1</sup> and in other studies done by Arun Roy et al<sup>2</sup> and Pagaro PM et al,<sup>3</sup> 11-30 years and 41-50 years age groups were involved respectively.

**Table 1:** Non Neoplastic lesions of lymphnode

S. No	Histopathological diagnosis	No of cases (%)
1.	Reactive	61(26%)
2.	Granulomatous – tuberculosis Others	35(15%) 14(07%)
3.	Kikuchi lymphadenitis	03(01%)
4.	Castleman’s disease	04(1.5%)
5.	Myeloid metaplasia	01(0.5%)
6.	Lipomelanotic lymphadenopathy	01(0.5%)
7.	Angiomatous lymphnodal hamartoma	01(0.5%)
	Total	120

**Table 2:** Neoplastic lesions of lymph node

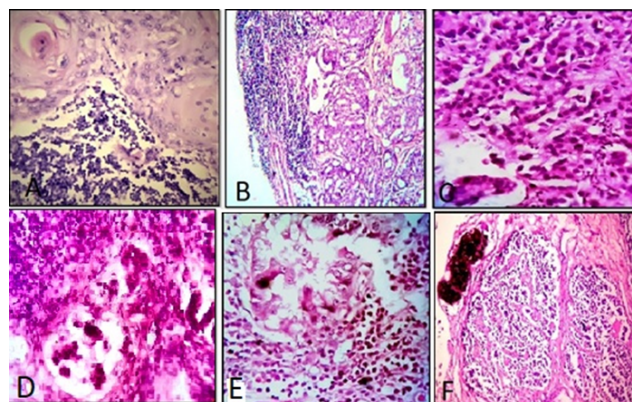
S. No	Type of lesion	No of cases (%)
1.	Metastatic deposits	47(20%)
2.	Non Hodgkin lymphomas	44(19%)
3.	Hodgkin lymphomas	19(9%)
	Total	110



**Fig. 1:** 1A: Lymph node showing multiple epithelioid granulomas with langhan's type of giant cells (H&E 100x), 1B: Kikuchi lymphadenitis showing necrosis and karyorrhexis (H&E 400x), 1C: Castleman's disease of hyaline vascular type characterized by prominent vascular proliferation and hyalinization of vessel walls. (H&E 400x), 1D: Angiomatous lymphnodal hamartoma (H &E 100x)

There was a slight female preponderance in the present study and male to female ratio was 1:1.1 which was correlating with studies done by Rajashri P et al,<sup>1</sup> Pagaro PM et al<sup>3</sup> and Mbata GC<sup>6</sup> et al where as in studies done by Arun Roy et al<sup>2</sup> Komal et al<sup>4</sup> and Hussain MI<sup>7</sup> et al male preponderance was seen.

The predominant site of lymph node biopsy was cervical followed by inguinal which was similar to studies done by Komal et al<sup>4</sup> Hussain MI et al,<sup>7</sup> Saraswat A et al<sup>8</sup> and

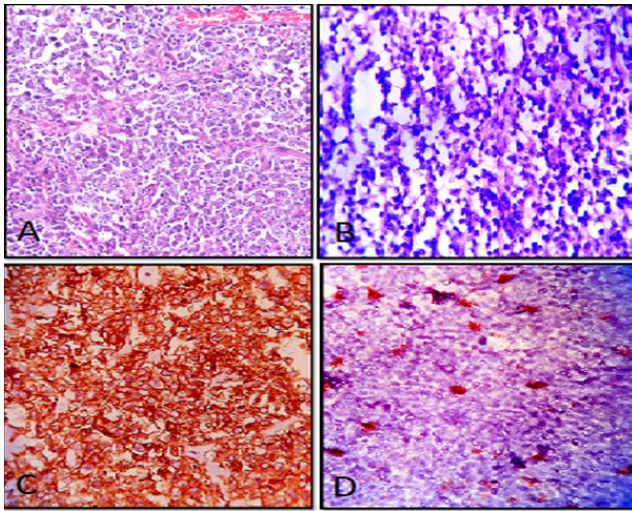


**Fig. 2:** 2A: Metastatic Squamous cell carcinoma of well differentiated type with keratin pearls (H&E 400x), 2B: Papillary carcinoma of thyroid metastasis showing papillary patterns and characteristic nuclear features (H&E 400x), 2C: Adenocarcinoma metastatic deposits in sheets and gland patterns (H&E 400x), 2D: Renal cell carcinoma metastatic deposit showing papillary patterns and cells with clear cytoplasm, vesicular nucleus and prominent nucleoli (H&E 100x), 2E: Metastasis from a Mucinous carcinoma showing pools of mucin with floating tumor cells (H&E 400x), 2F: Medullary carcinoma of thyroid metastatic deposits showing bands of fibrous tissue transecting the tumor and focal amyloid (H&E x100)

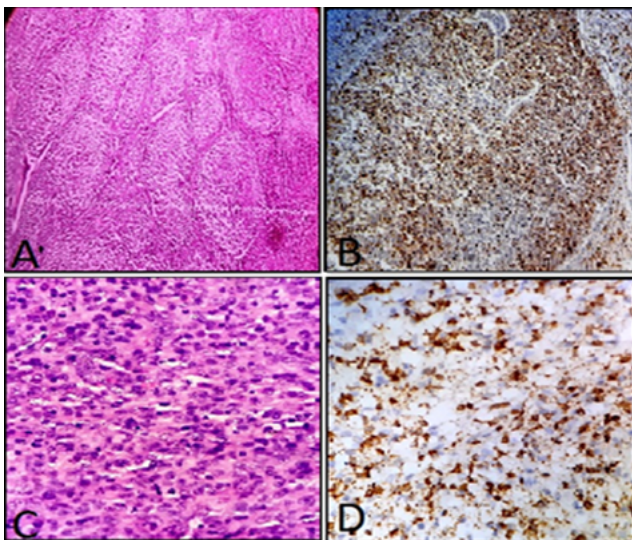
Rajashri P et al<sup>1</sup> and Khanday SA et al.<sup>9</sup> The preponderance of cervical lymphadenopathy may be related to its location near a common primary site of infections and malignancy that are drained through this single channel.<sup>10</sup>

In the present study non neoplastic lesions were more common compared to neoplastic lesions, and these results were consistent with studies done by Rajashri P et al<sup>1</sup> Komal et al<sup>4</sup> Saraswat et al<sup>8</sup> and Kamat GC et al<sup>11</sup> whereas neoplastic lesions were common in a study by Arun Roy

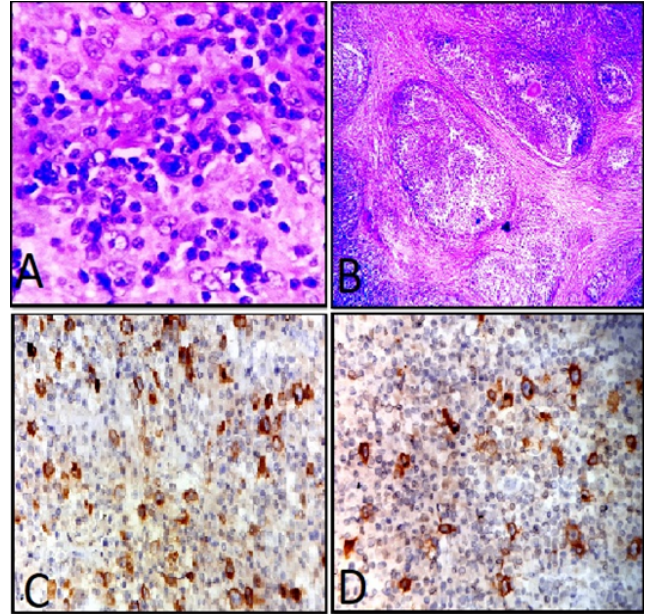




**Fig. 3:** 3A: Diffuse high grade non Hodgkin lymphoma showing lymphoid cells 2 to 3 times the size of small lymphocyte, vesicular nucleus and focal prominent nucleoli (H&E 400x), 3B: Small lymphocytic lymphoma showing a monotonous population of small lymphocytes (H&E 400x), 3C: IHC marker CD 20 showing diffuse and strong positivity in cytoplasm of cells in a B cell lymphoma (IHC CD 20 400x), 3D: IHC marker CD 3 negative in a B cell lymphoma (IHC CD 3 400x)



**Fig. 4:** 4A: Follicular lymphoma showing follicles with minimal size variation and with back to back arrangement (H&E 100x) , 4B: IHC marker Bcl2 positivity in >75% of lymphoid cells within the follicle ( IHC BCL2 100x), 4C: T cell lymphoma showing lymphoid cells with irregular nuclear membranes and vesicular nuclei (H&E 400x) , 4D: IHC marker CD3 showing positivity in cytoplasm of lymphoid cells in a T cell lymphoma (IHC CD 3 400x)



**Fig. 5:** 5A: Mixed cellular sub type of Hodgkin lymphoma showing mononuclear RS cells (H&E 400x), 5B: Nodular sclerosis sub type of Hodgkin lymphoma showing multiple nodules separated by collagen bands (H&E 100x) , 5C&D: IHC markers CD15 &CD 30 showing positivity in RS cells in mixed cellular sub type (IHC CD 15 & CD 30 400x)

et al.<sup>2</sup>

In the non neoplastic lesions reactive lymphadenitis was common as bacterial and viral infections can lead to reactive lymphadenopathy followed by tuberculous lymphadenitis. This was similar to studies done by Rajashri P et al<sup>1</sup> and Pagaro PM et al.<sup>3</sup>In studies done by Komal et al<sup>4</sup>and Hussain MI<sup>7</sup> et al tuberculous lymphadenitis was reported as the predominant cause of lymph nodal enlargement.

Metastatic deposits were common in neoplastic lesions accounting to 20%, followed by Non Hodgkin lymphomas (19%) and Hodgkin lymphomas (9%) this was similar to studies done by Rajashri P et al<sup>1</sup>and Pagaro PM et al<sup>3</sup>and Komal et al<sup>4</sup> whereas in studies done by Arun Roy et al<sup>2</sup>Non Hodgkin lymphomas were common followed by Hodgkin lymphomas and metastatic diseases.

Among the metastatic lesions most common type was Squamous cell carcinoma (20 cases). This was similar to a study done by Pagaro PM et al<sup>3</sup>and discordant with studies done by Rajashri P et al<sup>1</sup>and Arun Roy et al<sup>2</sup>where ductal carcinoma of breast and adenocarcinoma deposits were common respectively.

The second common type of metastatic lesion was papillary carcinoma of thyroid (13 cases) which was discordant with studies done by Rajashri P et al<sup>1</sup>and Arun Roy et al<sup>2</sup>

Age and gender play an important role in prognosis and treatment outcomes of lymphomas.

Non Hodgkin lymphomas comprised 44 cases (19%) and were found to be prevalent in 51-60 years age group. This was in accordance with a study by Vallabhajosyula et al<sup>12</sup> where the peak incidence was between 41-67 years and in a study by Roy et al<sup>2</sup> it was reported in 51-60 years age group.

In Non Hodgkin lymphomas, Diffuse large B cell lymphoma was the predominant type. This was similar to studies done by Rajashri P et al,<sup>1</sup> Arun Roy et al,<sup>2</sup> where as in a study done by Pagaro PM et al<sup>3</sup> follicular lymphoma was common. Immunologic characterisation of NHL B cell lymphomas are constantly more common worldwide.<sup>3</sup>

Mixed cellularity was the common subtype in Hodgkin lymphomas which was similar to a study done by Khanday SA et al,<sup>9</sup> whereas in study done by Arun roy et al<sup>2</sup> nodular sclerosis was the common subtype.

#### 4. Conclusion

The present study highlights the importance of lymph node biopsy and immunohistochemistry in establishing the cause for lymphadenopathy. In this study maximum number of cases were seen in the age group of 21-30 years and there was a female preponderance. In non – neoplastic lesions, reactive lymphadenitis was common followed by tuberculosis. In neoplastic lesions, metastatic diseases were common followed by Non Hodgkin lymphomas and Hodgkin lymphomas.

#### 5. Source of funding

None.

#### 6. Conflict of interest

None.

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