

Evaluation of Histopathological Findings in Lymph Node Lesions

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ABSTRACT

Introduction: Enlargement of lymph nodes is one of the most common presentations in inflammatory and neoplastic disorders. Persistent enlargement of lymph nodes requires detailed investigations to reveal an underlying pathology. Clinical features and radiology images may not be sufficient for diagnosing lymph node lesions. Hence, histopathology has become a mandatory tool to arrive at a definitive diagnosis.

Aim: To evaluate histopathological patterns of various lymph node lesions.

Materials and Methods: The present prospective study was undertaken in the Department of Pathology, Maharashtra Institute of Medical Sciences and Research, Latur, Maharashtra, India, from October 2016 to September 2018. Information regarding clinical history, and examination was noted from case sheet of patients. Total 104 lymph nodes were grossly examined and processed in routine paraffin technique and then stained with haematoxylin and eosin. Meticulous histopathological examination was done in each

case to arrive at correct histopathological diagnosis. Special stains and immunohistochemistry were performed wherever mandatory or indicated. Qualitative data was presented as frequency and percentages.

Results: Total 104 patients were studied, majority were males {n=56 (53.8%)} and mean age was 46 years. Reactive lymphadenitis was the most common cause of lymphadenopathy forming 60 (57%) cases. The metastatic lesions were in 23 (21.1%) cases. Other lesions encountered were tubercular lymphadenitis in 15 (14.3%) cases, diffuse large B-cell lymphoma in 3 (2.9%) cases, 58 (55.7%) patients had cervical lymphadenopathy and 35 (33.6%) patients had axillary lymphadenopathy.

Conclusion: Reactive lymphadenitis was the most common cause of lymphadenopathy in present study. Causes of lymphadenopathy can be suspected on clinical grounds, but histopathological examination is gold standard for early diagnostic and prognostic purpose. Special stains and immunohistochemistry should be done wherever mandatory or when indicated.

Keywords: Immunohistochemistry, Lymphadenitis, Lymphoma, Reactive, Tuberculous

INTRODUCTION

Enlargement of lymph nodes is a common clinical condition encountered by clinicians. A normal sized lymph node is <1 cm in diameter. Lymphadenopathy is the term used to describe the conditions in which lymph nodes become abnormal in size, consistency, or number, caused by the invasion or propagation of either inflammatory cells or neoplastic cells into the nodes [1]. Persistent enlargement of lymph nodes necessitates detailed investigations to reveal an underlying pathology. Although a reasonably accurate diagnosis can be made clinically, histopathological examinations are mandatory to establish and confirm the diagnosis [2].

It is important to take careful history to consider a variety of diseases, which may be a clue to the underlying pathology. The cervical region is the most frequent site involved in peripheral lymphadenopathy at any age. Lymphadenopathy is generally due to infections, but most often the supraclavicular lymphadenopathies are associated with malignancy [3].

Easy accessibility of acquiring a sample for cytological and histopathological examination has made it important component of practices of pathologists. Even though fine needle aspiration cytology has been introduced in the laboratory diagnosis since last two to three decades, there are still many situations, where excisional biopsies are mandatory, especially in suspected cases of lymphoproliferative disorders. Aim of the present study was to evaluate histopathological patterns of various lymph node lesions.

MATERIALS AND METHODS

This prospective cohort study was undertaken in the Department of Pathology, Maharashtra Institute of Medical Sciences and Research,

Latur, Maharashtra, India, from October 2016 to September 2018. The study was approved by the Ethical Committee of the Institute in the meeting held on 03/10/2016 (approval number-MIMSR/EC/28/2016, dated 08/11/2016).

Inclusion and Exclusion criteria: The patients of all age and sex diagnosed with lymphadenopathy with confirmation done on lymph node biopsy were included in the study. Inadequate specimen and individuals where only Fine Needle Aspiration Cytology (FNAC) was done without biopsy were excluded from this study.

Study Procedure

Total 104 lymph nodes were studied. Relevant patient data regarding age, sex, clinical details, results of imaging studies, and provisional diagnosis were retrieved from the patient request forms and records. The specimens were grossly examined for size, appearance, matting, consistency, and details of cut section and then fixed in 10% formalin for 24 hrs. The tissues were processed in routine paraffin technique and then stained with haematoxylin and Eosin (H&E). Slides were prepared and meticulous histopathological examination was done in each case to arrive at correct histopathological diagnosis. Finally, all data was subjected to analysis and interpretation to draw conclusions. Special stains and Immunohistochemistry were performed wherever mandatory or indicated.

STATISTICAL ANALYSIS

All the collected data were entered in Microsoft Excel sheet and then transferred to Statistical Package for Social Sciences (SPSS) software version 17.0 for analysis. Qualitative data was presented as frequency and percentages.

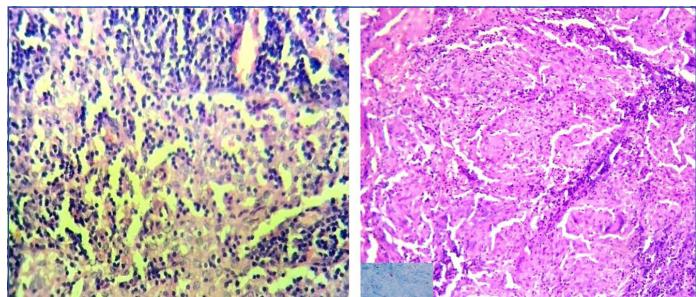
RESULTS

A total of 104 patients with lymph node lesions were included. Majority of the patients were from 41 to 60 years of age group 36 (34.6%), followed by 29 (27.9%) from 21-40 years of age group. Mean age was 46 years. Overall, 56 (53.8%) were males and 48 (46.2%) were females [Table/Fig-1]. Out of the 104 lymph nodes received for histopathological evaluation, a majority were from the cervical region comprising 58 (55.7%) cases followed by 35 (33.6%) cases in axillary region. The most common diagnosis was that of reactive lymphadenitis, followed by metastasis [Table/Fig-2]. In present study, reactive lymphadenitis was common cause of lymphadenopathy in all age group. While proportion of metastasis was found to be more in age group above 40 years i.e. 20 (64%) as compared to 3 (15%) below 40 years age [Table/Fig-3]. Reactive lymphadenitis (sinus histiocytosis) shows dilated sinuses containing increased macrophages and sinus lining cells [Table/Fig-4]. Out of the 15 cases of tubercular lymphadenitis, 6 (40%) were Acid-Fast Bacillus (AFB) positive. Tubercular lymphadenitis shows multiple caseating granulomas, among these few cases (40%) were AFB positive [Table/Fig-5]. Out of the five cases of lymphoma,

Age group (years)	Gender		Total (n,%)
	Female (n,%)	Male (n,%)	
≤ 20	2 (4.2%)	11(19.6%)	13 (12.5%)
21-40	13 (27.1%)	16 (28.6%)	29 (27.88%)
41-60	19 (39.6%)	17(30.4%)	36 (37.44%)
> 60	14 (29.1%)	12 (21.4%)	26 (27.04)
Total	48 (100%)	56 (100%)	104 (100%)

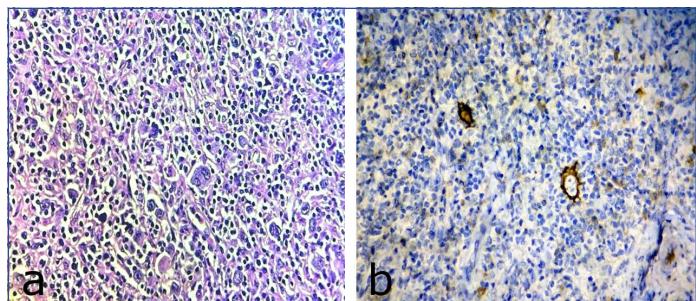
[Table/Fig-1]: Age and sex wise distribution of lymph node lesions amongst the study population.

one was Hodgkin's lymphoma (1%) [Table/Fig-6a] and the rest four were of Non Hodgkin's lymphoma (4%). All the cases of lymphoma were confirmed using immunohistochemistry. Hodgkin's lymphoma showed CD30 positivity [Table/Fig-6b]. Among the Non-Hodgkin's lymphoma three cases (2.9%) were of diffuse large B- cell lymphoma [Table/Fig-7a] which



[Table/Fig-4]: Sinus Histiocytosis showing dilated sinuses containing increased macrophages or sinus lining cells. (H&E x 40).

[Table/Fig-5]: Tuberculous Lymphadenitis Showing multiple caseating granulomas (H&E x 10) (Inset shows 20% AFB bacilli).



[Table/Fig-6]: a) Hodgkin's Lymphoma showing several diagnostic R-S cells admixed with polymorphous lymphoid infiltrate rich in eosinophils. (H&E X 40); b) Hodgkin's Lymphoma -Immunohistochemistry showing CD30 positivity in RS cells.

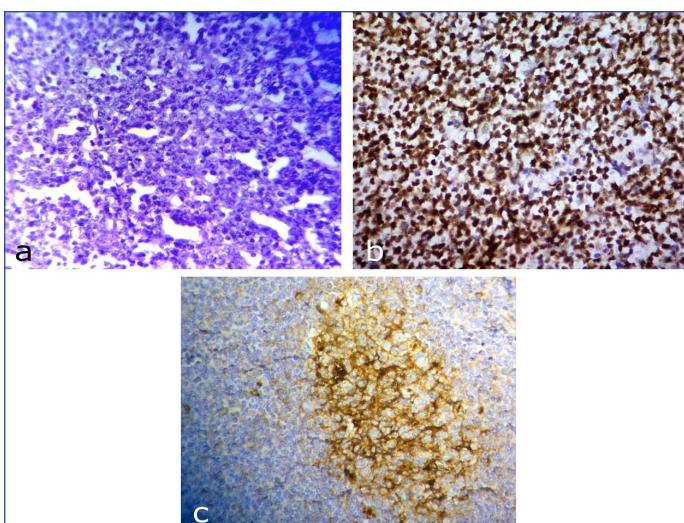
Biopsy diagnosis	Axillary (n,%)	Cervical (n,%)	Pelvic (n,%)	Mesenteric (n,%)	Paraileal (n,%)	Perigastric (n,%)	Inguinal (n,%)	Total (n,%)
Castleman's disease	0	1 (100%)	0	0	0	0	0	1 (100%)
Hodgkin's lymphoma	0	1 (100%)	0	0	0	0	0	1 (100%)
Metastasis	7 (30.4%)	9 (39.1%)	1 (4.3%)	4 (17.4%)	1 (4.3%)	1 (4.3%)	0	23 (100%)
Non Hodgkin's lymphoma (Diffuse large B-cell lymphoma)	2 (66.7%)	0	0	0	0	0	1 (100%)	3 (100%)
Non Hodgkin's lymphoma (follicular lymphoma)	0	1 (100%)	0	0	0	0	0	1 (100%)
Reactive lymphadenitis	21 (35%)	36 (60%)	1 (1.7%)	2 (3.3%)	0	0	0	60 (100%)
Tubercular lymphadenitis	5 (33.4%)	10 (66.7%)	0	0	0	0	0	15 (100%)
Total	35 (33.6%)	58 (55.7%)	2 (1.9%)	6 (5.8%)	1 (1.0%)	1 (1.0%)	1 (1.0%)	104 (100%)

[Table/Fig-2]: Distribution according to biopsy diagnosis and site of lymph node lesions amongst the study population.

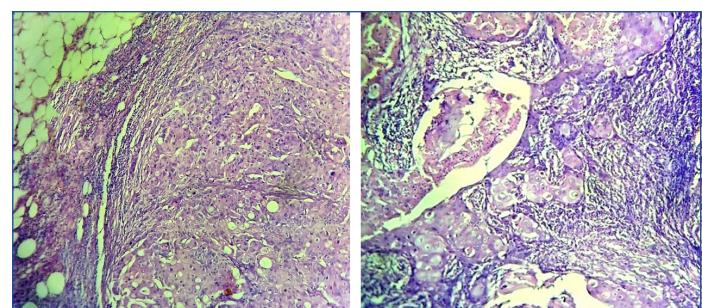
Biopsy diagnosis	Age group				Total
	≤20 years (n,%)	21-40 years (n,%)	41-60 years (n,%)	>60 years (n,%)	
Hodgkin's lymphoma	0	0	0	1 (4%)	1
Metastasis	1 (8%)	2 (7%)	12 (33%)	8 (31%)	23
Non Hodgkin's lymphoma (Diffuse large B-cell lymphoma)	0	1(3%)	0	2 (8%)	3
Non Hodgkin's lymphoma Non Hodgkin's	0	0	1 (3%)	0	1
Reactive lymphadenitis	10 (77%)	15 (52%)	22 (61%)	13 (50%)	60
Tubercular lymphadenitis	2 (15%)	10 (34%)	1 (3%)	2 (8%)	15
Total	13 (100%)	29 (100%)	36 (100%)	26 (100%)	104 (100%)

[Table/Fig-3]: Distribution according to age and biopsy diagnosis of lymph node lesions amongst the study population.

showed B-cell Lymphoma (BCL-6) and CD10 positivity [Table/Fig-7b,c]. One case was of follicular lymphoma (1%) [Table/Fig-8a] which showed CD 20 positivity [Table/Fig-8b]. Single case of Castleman's disease (1%) was seen [Table/Fig-9]. Out of 23 cases of metastasis majority of cases had infiltrating duct carcinoma (30.4%), followed by squamous cell carcinoma 6 (26.2%) cases [Table/Fig-10], 7(30.4%) cases of metastatic IDC showed nests and sheets of malignant ductal cells within lymph node. [Table/Fig-11]. Six cases (26.2%) of metastatic squamous cell carcinoma showed nests and clusters of atypical keratinized squamous cells within lymph nodes [Table/Fig-12]. Five cases (21.7%) of metastatic adenocarcinoma shows tumour cells arranged in glandular pattern within lymph node [Table/Fig-13]. One case (4.3%) of metastatic anaplastic carcinoma thyroid shows atypical large, bizarre cells within lymph node [Table/Fig-14]. Single case (4.3%) of metastatic poorly differentiated nasopharyngeal carcinoma showed diffuse sheets of tumour cells with round vesicular nuclei, prominent nucleoli and moderate amount of eosinophilic cytoplasm [Table/Fig-15].

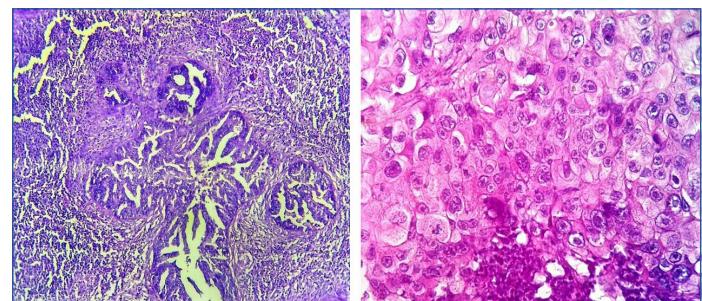


[Table/Fig-7]: a) Diffuse large B-cell lymphoma showing tumour cells arranged in diffuse sheets. Tumour cells have large vesicular nuclei with prominent nucleoli and abundant mitotic activity (H&E, 40X); b) Diffuse large B-cell lymphoma Immunohistochemistry showing BCL-6 positivity (H&E, 40X); c) Diffuse large B-cell lymphoma Immunohistochemistry showing BCL-6 positivity (H&E, 40X).



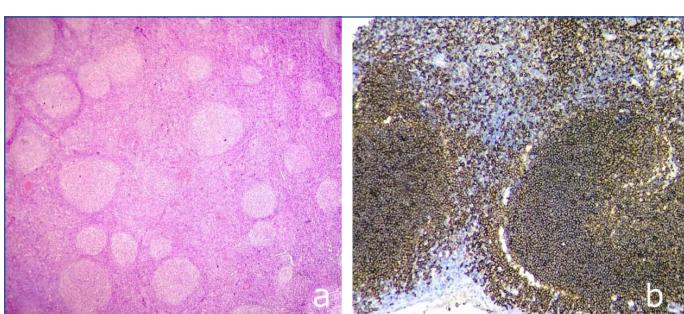
[Table/Fig-11]: Metastatic Invasive ductal carcinoma showing tumour cells arranged in nests and diffuse sheets within lymph node (H&E, 40X).

[Table/Fig-12]: Metastatic squamous cell carcinoma showing nests of atypical keratinized squamous cells within lymph node (H&E, 10X).

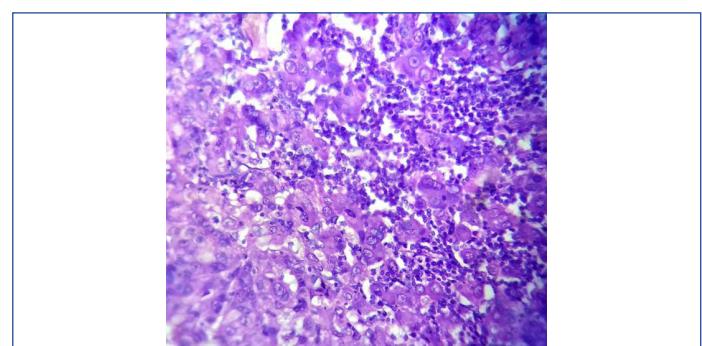


[Table/Fig-13]: Metastatic Adenocarcinoma showing tumour cells arranged in glandular pattern within lymph node (H&E, 40X).

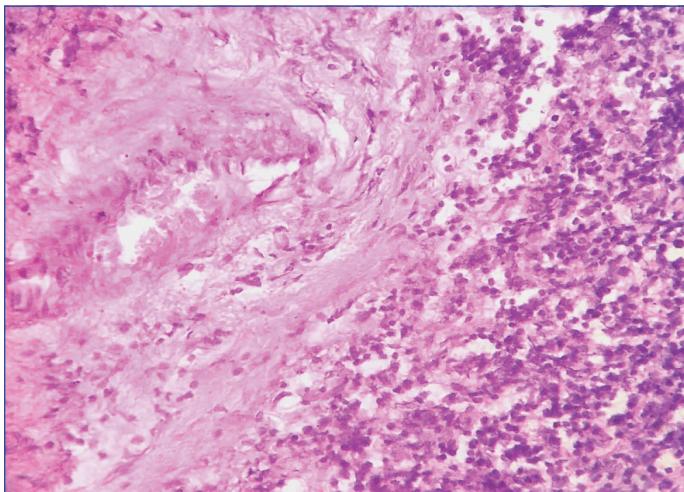
[Table/Fig-14]: Metastatic anaplastic carcinoma of thyroid to lymph node showing atypical giant and large cells within lymph node (H&E, 40X).



[Table/Fig-8]: a) Follicular lymphoma showing nodal effacement by closely packed follicles with attenuated or absent mantle zones. (H&E, 10X); b) Follicular Lymphoma- Immunohistochemistry showing CD20 positivity in lymphoid follicle (40X).



[Table/Fig-15]: Metastatic nasopharyngeal carcinoma showing tumour cells arranged in diffuse sheets within lymph node. Tumour cells have round vesicular nuclei, prominent nucleoli and moderate eosinophilic to amphophilic cytoplasm. (H&E X40).



[Table/Fig-9]: Castleman's Disease showing hyalinization of vessel walls with concentric layer of lymphocytes at the periphery resulting in an 'Onion skin' appearance (H&E, 40X).

Biopsy diagnosis	n,%
Adenocarcinoma	5 (21.7%)
IDC	7 (30.4%)
SCC	6 (26.2%)
Mucinous carcinoma	2 (8.8%)
Anaplastic carcinoma thyroid	1 (4.3%)
Poorly differentiated carcinoma	1 (4.3%)
Transitional cell carcinoma	1 (4.3%)
Total	23 (100%)

[Table/Fig-10]: Distribution of different subtypes of metastatic tumours amongst study population.

Site	Present study (%)	Damle R et al., [4] (%)	Murthy SA et al., [5] (%)	Shokouh TZ et al., [6] (%)	Pagaro PM et al., [7] (%)
Cervical	55.7	65.86	71	54.3	39
Axillary	33.6	15.76	10	25.5	-
Pelvic	1.9	-	-	-	0.5
Mesenteric	5.8	-	5	-	-
Paraileal	1	-	-	-	-
Peri gastric	1	-	-	-	-
Inguinal	1	1.75	10	9.6	-

[Table/Fig-16]: Comparison of site of lymph node lesions in present and other studies [4-7].

DISCUSSION

In present study, out of 104 lymph nodes received for histopathological evaluation, majority lymph nodes were from cervical region (55.7%), followed by 33.6% from axillary region and 5.8% were mesenteric lymph nodes. Study findings are consistent with the findings of Damle R et al., [4], Shivamurthy A et al., [5], Shokough TZ and Alireza A [6] and Pagaro PM et al., [7] [Table/Fig-16]. In present study, histopathological diagnosis of various lesions are most comparable to study done by Damle R et al., [4]. Prevalence of tubercular lymphadenitis was 14.3% [Table/Fig-11]. Ziehl-Nelsen (ZN) staining

was done in all the cases of tuberculous lymphadenitis and AFB positivity was shown by 40% which is comparable to Vimal S et al., (40.74%) and Chand P et al., (44.54%) studies [8,9]. The maximum AFB positivity was noted in cases with abundant necrosis (100%) comparable to Paliwal N et al., (85.5%) and Gupta AK et al., (78%) [10,11]. Out of 23 metastatic tumours 30.4% had Infiltrating duct carcinoma followed by 26.1% had squamous cell carcinoma and 21.7% had adenocarcinoma. 8.8% cases had mucinous carcinoma of rectum and 4.3% cases had each anaplastic carcinoma of thyroid, transitional cell carcinoma and poorly differentiated carcinoma.

Damle R et al., found that out of all metastatic lymph nodes, 34 (62.9%) cases were metastatic infiltrating breast carcinoma, 12 (22.2%) cases were metastatic squamous cell carcinoma, and 8 (14.8%) cases were metastatic adenocarcinoma [4]. Mbata GC et al., found in their study that most common cause of metastasis was breast cancer affecting mostly axillary lymph nodes [12]. Pagaro PM et al., found most common metastasis were metastatic squamous cell carcinoma (10.5%) followed by metastatic breast cancer (4.5%) [7]. Hemant B and Surekha H, found that out of all metastatic lymph nodes, 8 (34.8%) cases were metastatic infiltrating breast carcinoma, 6 (26.2%) cases were metastatic squamous cell carcinoma, and 4 (17.4%) cases were metastatic adenocarcinoma [13]. Two cases (8.7%) of metastatic papillary carcinoma of thyroid observed. One case (4.3%) each of metastatic nasopharyngeal carcinoma, small cell carcinoma of lung and undifferentiated carcinoma were observed.

Vachhani A et al., found that out of 23 metastatic lymph nodes, 9 (36%) cases were metastatic squamous cell carcinoma, 8 (32%) cases were metastatic IDC, and 3 (12%) cases were metastatic adenocarcinomas [14]. In comparison to various studies in the literature present study findings were similar to findings of Damle R et al., and Vachhani A et al., [4,14]. Malignancies have been the predominant cause of lymphadenitis in developed countries than developing countries like India because of racial and genetic factors. Study by Roy A et al., and Mohan A et al., constituted 44.5% and 25.9% cases of lymphoma which were very higher incidence than the present study. Because, these studies included large number of cases and conducted in Research Centre or Oncology Institute [15,16]. The reactive lymphadenitis was most common pathologic finding observed in most of the other studies and in present study [Table/Fig-17] [4,5,7,13,16-19].

Name of authors	Metastasis (%)	Reactive lymphadenitis (%)	Tubercular lymphadenitis (%)	Castleman's disease (%)	Hodgkin's lymphoma (%)	Non-Hodgkin's lymphoma (%)
Present study, 2019	22.1	57.7	14.3	1	1	3.9
Egejuru RO et al., 2018 [17]	50	17.86	14.29			8.9
Pagaro PM et al., 2017 [7]		34.5	20.5			35.5
Hemant B et al., 2017 [13]	9		32.1			11
Damle R et al., 2017 [4]	16.31	52.87	20.24	0.9	1.2	2.4
Shivamurthy A et al., 2016 [5]	38	15	16	1	2	22
Vachhan A et al., 2013 [14]	23	51				2
Kamat GC, 2011 [18]	7.37	30.73			0.4	3.27
Melkundi R et al., 2017 [19]	20	24	52		2	2

[Table/Fig-17]: comparison of biopsy diagnosis of lymph node lesions in present and other studies [4,5,7,13,16-19].

Limitation(s)

As lymphadenopathy is common finding for the physician in day-to-day practice and initial test used for diagnosis is FNAC and the patients were treated accordingly, hence the sample size of study was limited.

CONCLUSION(S)

While evaluating the histological pattern of lymph nodes in various age groups it was found that, in general reactive lymphadenitis was the most common cause of lymphadenopathy in all age groups but proportion of metastasis was more in age group above 40 years. The most common groups of lymph nodes involved were cervical group of lymph nodes followed by the axillary. Causes of lymphadenopathy can be suspected on clinical grounds, but histopathological examination helps in categorising the causes of lymph node enlargement as reactive changes, infective/inflammatory, lymphoma, and metastasis. So it is concluded that, lymph node biopsy is an important tool for early diagnostic and prognostic purpose.

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