

Histopathological Evaluation of Lymph Node Biopsies: A Hospital Based Study

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Abstract

Background: Lymphadenopathy is a common manifestation of a large variety of disorders, both benign and malignant. It is essential to define the pattern of disorders presenting primarily as lymph node enlargement in a particular environment. Histopathological examination of the lymph node biopsies is a gold standard test in the distinction between reactive and malignant lymphoid proliferations as well as for detailed subtyping of lymphomas. We designed this study in our population for histopathological evaluation of lymph nodes that might be helpful for clinical management of these lesions. **Objective:** Histopathological evaluation of lymphadenopathy from excised specimen, in relation to age and sex of the patients, and distribution of the lymph nodes. **Materials and Methods:** It was a retrospective cross sectional study conducted in the department of Pathology, Enam Medical College & Hospital, Savar, Dhaka during the period from January 2006 to December 2010. Lymph node biopsies of all patients of both sexes and all age groups were included. Metastatic lymph nodes associated with evidence of primaries elsewhere in the body were excluded from the study. Total 191 lymph node biopsies were selected for histopathological evaluation. Among these 90 (47.12%) were from males and 101 (52.88%) were from females with male to female ratio being 1:2.1. The age of the patients ranged from 2 to 85 years with a mean age of 35.73 ± 18 years. **Results:** Cervical lymph nodes were the most common (56%) biopsied group. Of the 191 cases 59 cases (30.89%) were reactive lymphadenitis, 64 cases (33.5%) were tuberculosis, 2 cases (1.05%) were non-caseous granuloma, 11 cases (5.76%) were Hodgkin lymphoma, 22 cases (11.52%) were non-Hodgkin lymphoma, 24 cases (12.57%) were metastatic neoplasm and 9 cases (4.7%) were other lesions. **Conclusion:** Tuberculosis was the most common cause of lymphadenopathy, followed by reactive lymphadenitis and the cervical group of lymph nodes was most frequently affected.

Keywords: Tuberculosis, Hodgkin lymphoma, Non-Hodgkin lymphoma, Metastatic neoplasm

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Introduction

Lymph nodes are discrete ovoid lymphoid structures that are widely distributed throughout the body. Lymphadenopathy refers to nodes that are abnormal in size, consistency or number, caused by the

invasion or propagation of either inflammatory cells or neoplastic cells into the nodes.

Clinically, lymphadenopathy may be peripheral or visceral. Peripheral lymphadenopathies are easily

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detected by routine physical examination and are often biopsied as they are easily accessible for lymphadenectomy, which is a minor surgical procedure. Visceral lymphadenopathy on the other hand, requires laparotomy or sophisticated imaging techniques for detection.

Among the peripheral nodes, those in the upper part of the body (cervical, supraclavicular, axillary) are preferentially biopsied than lower limb nodes (popliteal, inguinal or femoral) as the former are more likely to yield definitive diagnosis whereas the latter are often characterized by non-specific reactive or chronic inflammatory and fibrotic changes.^{1,2}

Lymphadenopathy is a common clinical problem, and biopsies are usually undertaken to determine the cause of nodal enlargement. Various reports document tuberculosis and infectious etiology as major causes of lymph node enlargement,^{3,4} whereas malignancies as a predominant cause in the developed countries.^{5,6} Increase in incidence of tuberculosis attributed to the advent and preponderance of HIV infection has been documented worldwide.^{7,8,9}

Considering the plethora of diseases that may cause lymphadenopathy, it is essential to define the pattern of disorders presenting primarily as lymph node enlargement in a particular environment.¹⁰ Pattern of lymph node enlargement is different in different age group. Metastatic deposit is common in adults whereas it is rare in children.^{11,12} Reactive hyperplasia to minor stimuli has been reported as a significant cause of lymphadenopathy in children.¹³

The intent of this study was etiological evaluation of lymphadenopathy, in relation to age and sex of the patients and pattern of lymph node distribution in lymph node biopsy samples received in the department of Pathology, Enam Medical College & Hospital.

Materials and Methods

This is a retrospective cross sectional study of lymph node biopsies conducted in the department of Pathology of Enam Medical College & Hospital, Savar, Dhaka during a period of 5 years, from January 2006 to December 2010. A total of 191 lymph node biopsies were selected for

histopathological evaluation. Histology slides of all cases were reviewed and clinicodemographic data regarding age, sex, anatomical site of nodal biopsy and clinical information were obtained from histology request forms and register. All biopsies were fixed in 10% formalin and routine hematoxyline-eosin stained sections were examined. Special stains like Ziehl-Neelsen and Periodic Acid-Schiff stains were employed where necessary.

Lymph node biopsies (e.g., cervical, axillary, inguinal, abdominal) of all patients of both sexes and all age groups were included. Metastatic lymph nodes associated with evidence of primaries elsewhere in the body, e.g., axillary nodes in breast carcinoma or lymph nodes sent as part of main specimen such as surgery of bowel and gall bladder were not included in this study. Only one biopsy per patient was included. Results were interpreted in respect of age, sex and site of lymphadenopathy on the basis of histopathological diagnosis.

Non-Hodgkin lymphomas (NHLs) were classified based on working formulation. Diagnosis of tuberculosis was confirmed by demonstration of epithelioid granuloma with caseation necrosis on histopathological examination. The results were tabulated and presented as percentage frequencies. Means and standard deviations (SD) were used to summarize continuous variables, while percentages were used for categorical variables.

Results

A total of 191 lymph node specimens were received in the department of Pathology, Enam Medical College & Hospital, Savar, Dhaka from 2006 to 2010, accounting for 4% of all surgical biopsy specimens examined. There were 90 (47.12%) males and 101 (52.88%) females with male to female ratio being 1:2.1. The age of the patients ranged from 2 to 85 years with a mean age of 35.73 ± 18 years. The mean age of male patients was 35.44 ± 20.73 years and that of the female patients was 35.79 ± 15.28 years. Most of the patients were in the 3rd decade (22%) followed by 4th decade (17.8%) of life (Fig 1). Amongst males, maximum number of cases (16.7%) were in 4th decade, while amongst females, maximum number of cases (28.7%) were in the 3rd decade of life.

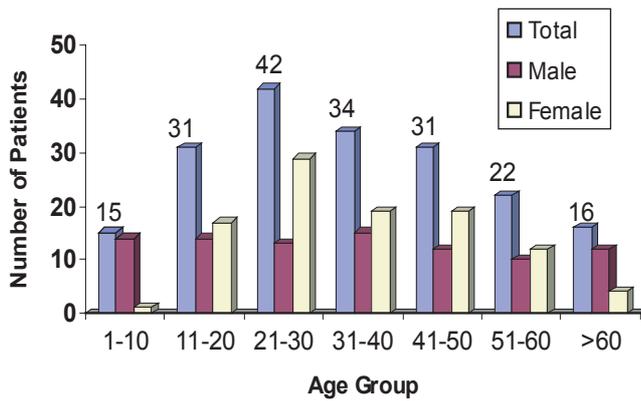


Fig 1. Age and sex distribution of the patients

Cervical lymph nodes were the most commonly biopsied group (56%), followed by axillary, abdominal and inguinal group of lymph nodes (Table I). The overall diagnostic yield in 191 biopsies was 64.4% with abdominal lymph nodes giving the highest yield (67.9%) and the submental group giving the least diagnostic yield. Among the different spectrum of lesions, 65.2% cases of TB, 57.6% of reactive lesions, 42.4% of lymphoma, 50% of metastatic neoplasms and 44.4% of other specific causes of lymphadenitis were found in the cervical group of lymph nodes.

Table I: Distribution of various histopathologic diagnoses according to lymph node location and diagnostic yield in each group

Lymph node location	Total number (%)	Reactive	TB	Non caseous granuloma	Lymphoma		Metastatic neoplasm	Other lesions	Diagnostic yield (%)
					HL	NHL			
Cervical	107 (56)	34	41	2	6	8	12	4	64.5
Submental	1 (0.5)							1	0
Submandibular	5 (2.6)	3			1	1			40
Supraclavicular	7 (3.7)	2	4					1	57.1
Axillary	31 (16.2)	7	9		2	5	5	3	67.7
Inguinal	12 (6.3)	4	3		2	2	1		66.7
Abdominal	28 (14.7)	9	7			6	6		67.9

TB=Tuberculosis; HL=Hodgkin lymphoma; NHL=Non-Hodgkin lymphoma

Diagnostic yield of each group is defined as: (Number of biopsies with specific histopathologic findings in this group/Total number of biopsies of the same group) × 100

Distribution of various histological diagnoses, mean age values and sex distribution are shown in Table II. In this study, non-neoplastic lesions were more common comprising 70.16% (134 cases). TB was the most common cause of lymphadenopathy and accounts for 47.76% of all non-neoplastic lesions.

Females were more frequently affected compared to males with a female to male ratio of 1.78:1. Most of the patients (n=51; 79.7%) were between 11-40 years of age (Table III). Caseous granuloma was found in all of these cases. Noncaseating granuloma was seen in only two biopsies.

Table II: Age and sex distribution of 191 patients with lymphadenopathy

Diagnosis	Total number (%)	Gender			Age (Year)	
		Male	Female	M:F	Range	Mean ± SD
Reactive	59 (30.89)	29	30	1:1.03	2-80	34.32 ± 20.87
TB	64 (33.5)	23	41	1:1.78	10-75	31.22 ± 13.72
Non-caseous granuloma	2 (1.05)	1	1	1:1	19-38	28.50 ± 13.44
HL	11 (5.76)	10	1	10:1	30-85	53.09 ± 19.09
NHL	22 (11.52)	14	8	1.75:1	5-65	36.23 ± 19.02
Metastatic neoplasm	24 (12.57)	11	13	1:1.2	17-65	46.04 ± 12.44
*Other lesions	9 (4.7)	2	7	1:3.5	12-45	26.56 ± 13.09
Total	191	90	101	1:2.11	2-85	35.73 ± 18.00

*detailed in the text under Results

Table III: Histological diagnosis and age of 191 patients with lymph node biopsies

Age	Non-neoplastic lesion (n=134; 70.16%)				Neoplastic lesion (n=57; 29.8%)		
	Reactive	TB	Non-caseous granuloma	Other lesions	HL	NHL	Metastatic neoplasm
1-10	11	2				2	
11-20	5	16	1	4		5	1
21-30	14	20		2	2	2	2
31-40	6	17	1	1	2	2	6
41-50	10	5		2	2	6	6
51-60	6	3			1	4	8
>60	7	3			4	1	1
Total	59	64	2	9	11	22	24

Reactive lymphadenitis was the second most common cause of lymphadenopathy and accounts for 44% of all non-neoplastic lesions. Out of 59 cases, 30 (50.8%) were follicular hyperplasia, 19 (32.2%) were sinus histiocytosis and 10 (16.9%) were chronic non-specific lymphadenitis.

Malignancies comprised 29.8% (57 cases) of enlarged lymph node with lymphomas predominating accounting for 17.3%, making them collectively the third most prevalent cause of lymphadenopathy in this series. Among the lymphomas, non-Hodgkin lymphomas (NHLs) were more common with intermediate and high grade types being predominant (Table IV). Hodgkin lymphoma was predominantly observed in males (Table II). Mixed cellularity type was the most common subtype, seen in 7 cases (63.6%), followed by lymphocyte predominance and nodular sclerosis types (Table IV).

Metastatic neoplasm accounts for 42.1% of malignant lesions. Among the various types of tumors metastasizing the lymph nodes, adenocarcinoma was the commonest comprising 37.5% (9 cases), followed by squamous cell carcinoma (n=6; 25%), breast cancer involvement of axillary nodes (n=5; 20.8%), poorly differentiated carcinoma (n=2; 8.3%), papillary carcinoma of the thyroid gland (n=1; 4.2%) and nasopharyngeal carcinoma (n=1; 4.2%).

Table IV: Nodal lymphomas in 33 patients

Morphologic types	No of cases (% for group)
Non-Hodgkin lymphoma	
Low grade	2 (9.2)
Intermediate grade	14 (63.6)
High grade	6 (27.2)
Total	22 (100)
Hodgkin lymphoma	
Nodular sclerosis	1 (9.1)
Mixed cellularity	7 (63.6)
Lymphocyte predominance	3 (27.3)
Lymphocyte-rich	-
Lymphocyte depletion	-
Total	11 (100)

Other patterns of lymphadenopathies were identified in 9 cases (4.7%) comprising of 5 cases of acute lymphadenitis, 3 cases of Kikuchi's necrotizing lymphadenitis and 1 case of necrotic foci with neutrophils suggestive of cat-scratch disease (Table II).

Discussion

Patients presenting with enlargement of the lymph nodes is one of the most common problems in clinical practice.¹⁴ Lymphadenopathy offers an important diagnostic clue to the etiology of the underlying condition. The cause of lymphadenopathy often cannot be ascertained on clinical grounds alone. Excision biopsy of the lymph node provides material to establish an early diagnosis and is a vital part of the management.¹⁵

In this study, cervical lymph nodes were the most frequently biopsied constituting 56% of nodal biopsies. This is consistent with virtually all other lymph node studies.^{15,16} Next common group includes axillary and abdominal lymph node biopsies which comprised 14.7% and 14.13% respectively. The overall diagnostic yield of lymph node biopsy was 64.4%. A study done by Morad N et al¹⁷ revealed diagnostic yield of 67% with supraclavicular lymph nodes giving the highest yield of 80%. In our study highest diagnostic yield (67.9%) was found with abdominal lymph nodes and supraclavicular lymph nodes gave 57.1% yield.

In agreement with other studies benign lesions were more frequent comprising 70.2% of lymph node enlargement and malignant lesions constituted 29.8%.^{15,16} In contrast, a study

done by Olu-Eddo AN et al¹⁰ revealed malignancy being the predominant lesion constituting 55% of cases. The higher incidence of malignant tumors are also documented in the western series.^{5,6,18}

Tuberculosis was the commonest cause of lymphadenopathy in this study accounting for 33.5%. Tuberculosis has also been reported by several authors as the predominant lesion in adults in the tropics.^{3,4} The studies performed in other developing countries also showed TB lymphadenitis being the most common cause of lymphadenopathy.^{16,19,20} The high incidence of TB has been attributed to the low socio-economic status and the attendant poor standard of living in the third world countries.²¹

In the western countries, infections like TB have become rare and malignancies including lymphoma are the predominant causes of lymph node enlargement.^{5,6} The higher rates of tuberculosis in some African countries like Zambia is due to their higher HIV infection rates, tuberculosis being an AIDS-defining illness.⁸ Different other studies also revealed predominance of TB due to higher HIV infection.⁹ In the last three decades, HIV/AIDS has also been responsible for the resurgence of tuberculosis. Coincident with the AIDS epidemic, the incidence of tuberculosis has risen dramatically. Worldwide, almost a third of all deaths in AIDS patients are attributable to tuberculosis. Prior to the HIV pandemic, tuberculosis was declining due to improved living standards.⁷ We could not analyze the HIV status in patients with TB because test for HIV was not done.

In this study, TB affected mainly the cervical group of lymph nodes of young adult females with maximum at 21-30 years and 80% of the patients were between 11-40 years of age. Only 11% patients with TB lymphadenitis were above 40 years of age. These results are consistent with the findings of other authors.^{3,4,10,21} A study from Turkey showed that the most common site of extrapulmonary TB lymphadenitis was intrathoracic lymph nodes followed by cervical lymph nodes.²²

Like Asian and North African populations, in the USA tubercular lymphadenitis was found to be more common in females as compared to males.²³ Two cases of granulomas lacking caseation or other

specific features were seen in this review. These possibly were early tuberculosis before the development of caseous necrosis. Both of these were negative for acid-fast bacilli (AFB).

Reactive lymphadenopathy was the second most common cause in this study and accounts for 30.89% of lymph node lesions. Out of 59 cases, 50.8% were follicular hyperplasia, 32.2% sinus histiocytosis and 16.9% chronic non-specific lymphadenitis. This is similar to the findings of Kamat GC²⁰ where reactive lymphadenitis was also the second common cause of lymphadenitis next to TB (30.73% and 58.19% respectively). This included 75 cases of reactive lymph nodes, 69.3% were follicular hyperplasia, 21.4% sinus histiocytosis, and 9.3% paracortical hyperplasia. These results differ from that of Attah EB²⁴, Sibanda et al²⁵ and Moore et al²⁶ who found reactive change highest followed by TB. Attah EB reported 33% of reactive change and 30% of TB, Sibanda et al found 33% of reactive change and 26.7% of TB and Moore et al found 47.8% of reactive lesions and 36.3% cases of TB.

Malignant tumors constituted 29.8% cases with lymphoma accounting for 17.3%, making them collectively the third commonest cause of lymphadenopathy. These are consistent with the findings of other authors.^{10,17,18} However, some other authors found predominance of metastatic neoplasms among the malignancies.^{15,20} Among the lymphomas, NHLs were more common comprising 11.5% of lymphadenopathies while HL constituted 5.76%. Other studies also document a preponderance of NHL over HL.^{10,15} In the western world NHL is reported to be three to four times more common than HL. The much higher proportion of NHL in the western world may be partly explained by racial and genetic factors.²⁷

Intermediate and low grade lymphomas accounted for over 80% NHL in the USA²⁷, whereas high and intermediate grades were predominant in our study comprising 91%. In contrast to these studies, Naseem SS et al¹⁹ found predominance of HL over NHL (72 cases versus 27 cases).

Hodgkin lymphoma showed marked predilection for the cervical group of lymph nodes with a striking male to female ratio of 10:1. These findings corroborate with other findings.^{4,10} The mixed

cellularity type is the most common pattern in the current study, in agreement with other studies.^{17,19}

In the present study, metastatic tumors was the fourth commonest cause of lymphadenopathy constituting 12.57% cases, which is similar to the study of Shrestha AK et al.¹⁶ In agreement with others, majority of the patients (62.5%) were above the age of 45 years.^{4,16} Out of 24 metastatic lesions, adenocarcinoma and squamous cell carcinomas were common comprising 37.5% and 25% respectively. The distribution of metastatic lymph nodes among both sexes depends upon the tumor type (primary), as metastatic lymph nodes in patients with breast carcinoma will be seen more in female patients and vice versa.¹³

The varied etiology of lymphadenopathy observed at our tertiary care center, as documented by histopathological evaluation, was comparable to studies conducted in other developing countries. TB was the most common cause of lymphadenopathy, followed by reactive lymphadenitis and presented mostly with cervical lymphadenopathy. Females were frequently affected by TB as compared to males. In both HLs and NHLs males were frequently affected than females. Among the HLs, mixed cellularity was the commonest subtype and among the NHLs, intermediate grade lymphomas were more common. Among metastatic tumors, adenocarcinoma and squamous cell carcinoma were frequent.

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