

## Profile of Lymphadenopathy: An Institutional Based Cytomorphological Study

### Abstract

**Introduction:** Lymphadenopathy is one of the most common clinical presentations of patients attending the outdoor department of a hospital. Lymph node aspiration is of great value for the diagnosis of lymphadenitis, lymphomas, and metastatic carcinoma. **Materials and Methods:** In this study, we have reported the pattern of cytological diagnosis on fine-needle aspiration cytology (FNAC) of lymphadenopathy cases in Jammu region of Jammu and Kashmir state of India. The mean age of all the patients in this study was 21.67 years. The most common site of lymphadenopathy was cervical region (71.79%) followed by axillary region (11.11%). **Results:** Tubercular lymphadenitis (44.02%) was the single most common cause of lymphadenopathy followed by reactive lymphadenitis (42.64%), metastatic lesions (9.40%), and malignant lymphoma (4.70%). The sensitivity of 94.49%, positive predictive value of 96.26%, and diagnostic accuracy of 91.15% was achieved in our study. **Conclusion:** This study highlights the role of FNAC as a simple, inexpensive, relatively painless, rapid, repeatable, and reliable method of investigation for lymphadenopathy, especially in outpatient departments, peripheral hospitals, and dispensaries.

**Keywords:** Fine-needle aspiration cytology, lymphadenitis, lymphadenopathy

### Introduction

Lymphadenopathy is the enlargement of a lymph node and lymphadenitis is the inflammation in a lymph node. Lymphadenopathy is one of the most common clinical presentations of patients attending the outdoor department of a hospital. Lymph nodes comprise an important part of the defense system of the human body. They are small, rounded, or kidney-shaped nodules of lymphoid tissue that perform nonspecific filtration of particulate matter and micro-organisms from lymph. They become secondarily involved in virtually all infectious diseases and in many neoplastic disorders, lipid storage diseases, endocrine disorders and in many miscellaneous conditions such as sarcoidosis and histiocytosis. Lymph node aspiration is of great value for the diagnosis of lymphadenitis, lymphomas, and metastatic carcinoma. Fine-needle aspiration cytology (FNAC) is a safe, reliable, rapid, and inexpensive method of establishing the diagnosis of a lesion and also helps in indicating the pattern of the investigation.<sup>[1]</sup> The knowledge of the pattern of lymphadenopathy in a given

geographical region is essential for making a confident diagnosis or suspecting a disease. Tuberculosis is the most common cause of lymphadenopathy in developing countries like India and should be considered in every case of granulomatous lymphadenopathy unless proved otherwise.<sup>[2]</sup> In children and young adults, lymphadenopathy is generally due to viral or bacterial infections whereas malignant disorders form the major cause of lymphadenopathy in those aged above 50 years. Localized or regional lymphadenopathy is frequently associated with viral infections, toxoplasmosis, connective tissue disorders, systemic lupus erythematosus, acute lymphoblastic leukemia, chronic lymphocytic leukemia, and lymphomas.

The present randomized study was undertaken to study the etiopathology of nonneoplastic and neoplastic lesions of enlarged lymph nodes by FNAC along with the study of their morphological patterns in patients presenting with lymphadenopathy in the Department of Pathology of Acharya Shri Chander College of Medical Sciences, Jammu over a period of 1 year to determine the pattern of disease affecting lymph nodes in this region.

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## Materials and Methods

This study comprises 238 patients of all ages presenting with enlarged lymph nodes who were referred to our Department of Pathology by the clinicians in outpatient department (OPD) of a tertiary care hospital in Northern India, over a period of 1 year. In each instance, a brief clinical history and physical examination along with an evaluation of relevant investigations, if available, was carried out. The FNAC procedure was performed under strict asepsis using a Franzen's aspiration handle using 23/24-gauge needles attached to a 20 ml syringe. Multiple sites were aspirated. The aspirated material was smeared onto four slides in each case. Two slides were immediately immersed in 95% ethanol and remaining air-dried. The air-dried smears were routinely stained by May-Grunwald-Giemsa stain and alcohol fixed smears stained by hematoxylin and eosin stain and Papanicolaou stain. Special stains like Ziehl-Neelsen stain (ZN) stain for acid-fast bacilli (AFB) and periodic acid-Schiff for mucin were done whenever required. The diagnosis was classified according to various morphological patterns and correlated clinically. In 113 cases (48.20%) cytology and histopathology correlation were available. Standard guidelines for cytological diagnosis were followed as far as practicable. Data were analyzed using a computer software Epi Info version 6.2 (Atlanta, Georgia, USA) and Microsoft Excel for Windows.

## Results

A total of 238 cases were subjected to FNAC of which 234 cases (98.31%) yielded adequate material for interpretation and four cases yielded inadequate material. Of these, 113 (48.29%) were followed by histopathological examination. In 218 (93.16%) patients, aspiration was done from palpable superficial lymph nodes while 16 (6.83%) were deep-seated.

### Age and gender

The age of the patients ranged from 4 months to 78 years. The mean age of all the patients presenting with lymphadenopathy was 21.67 years. The mean age for benign lesions was 20.09 years and for malignant lesions was 45.48 years. 56.40% of patients with benign lesions were below 20 years of age, whereas 50.78% of cases with FNA diagnosis of malignancy were above 50 years of age. In general, a male-to-female ratio of 1.2:1 was observed, with males contributing 128 cases (54.70%) and females 106 cases (45.29%) [Table 1].

### Number and site

Eighty-nine (39.73%) patients had solitary lymphadenopathy and 135 (62.26%) patients had multiple enlarged lymph nodes. Cervical region was found to be the most common site of lymphadenopathy (168 cases, 71.79%) followed by axillary region (26 cases, 11.11%), inguinal region (15 cases,

6.41%), abdominal region (11 cases, 4.70%) and mediastinal region (4 cases, 1.79%) [Table 1]. Deep-seated lesions were aspirated under image guidance (both computed tomography and ultrasonography). Of the 168 patients with cervical lymphadenopathy, 44 (26.19%) had sub-mandibular lymph nodes, 16 (9.52%) had supraclavicular, and 6 (3.57%) had submental lymph nodes.

### Size

The size of the lymph nodes was <1 cm in 15 (6.41%) cases and ranged from 1 to 3 cm in 183 cases (78.20%) and >3 cm in remaining 35 cases (14.95%).

### Diagnosis

The cytological features were observed to be benign in 202 cases (86.32%), and malignant in 32 cases (13.68%). Overall, tubercular lymphadenitis (103 cases, 44.02%) was the single most common cause of lymphadenopathy. The next common causes were reactive lymphadenitis (98 cases, 42.64%), metastatic lesions (22 cases, 9.40%), and malignant lymphoma (11 cases, 4.70%).

In males, the most common cause of lymphadenopathy was found to be reactive lymphadenitis, (61 cases, 47.6%) followed by tubercular lymphadenitis (45 cases, 35.15%), metastatic lesions 14 cases (10.93%), and malignant lymphoma (6 cases, 4.6%). Whereas in females, the most common cause was tubercular lymphadenitis (58 cases, 54.72%) followed by reactive lymphoid hyperplasia, (37 cases, 34.90%), metastatic lesions (8 cases, 6.25%), and malignant lymphoma (5 cases, 3.91%) [Figure 1].

In cases with tubercular lymphadenitis, epithelioid cells were present in 76 cases (73.79%) and Langhans giant cells were detected in 38 cases (36.89%) [Figure 2]. Cytological features were described under three major categories: Epithelioid granuloma without necrosis (29 cases, 28.16%), epithelioid granuloma with necrosis (47 cases, 45.63%) and necrosis without epithelioid granuloma (27 cases, 26.21%). ZN staining for AFB was performed and forty cases (38.83%) were positive.

**Table 1: Incidence of lymphadenopathy in relation to various regions and sex**

Lymph node region	Male, n (%)	Female, n (%)	Total, n (%)
Cervical	91 (71.09)	77 (72.64)	168 (71.79)
Axillary	12 (9.38)	14 (13.21)	26 (11.11)
Mediastinal/hilar	2 (1.56)	2 (1.89)	4 (1.79)
Abdominal	6 (4.69)	5 (4.72)	11 (4.7)
Inguinal	10 (7.81)	5 (4.72)	15 (6.41)
Two lymph node region	3 (2.34)	2 (1.89)	5 (2.14)
Generalized	4 (3.13)	1 (0.93)	5 (2.14)
Total	128 (100)	106 (100)	234 (100)

Four cases (1.71%) were diagnosed with Hodgkin's lymphoma [Figure 3] while seven cases (2.99%) were diagnosed with non-Hodgkin lymphoma (NHL). Subtyping of Hodgkin's lymphoma showed nodular lymphocyte predominant type in 50% of cases, lymphocyte rich type in 25% of cases and lymphocyte depleted type in 25% of cases. Subtyping of NHL cases (KIEL classification) showed lymphoblastic type in 28.55% of cases and centroblastic/centrocytic type, immunoblastic type, burkitt type, lymphoplasmacytic type, and malignant lymphoma; not otherwise specified (NOS) in 14.29% cases each.

Nine cases (3.87%) were diagnosed as adenocarcinoma, six cases (2.56%) as squamous cell carcinoma, two cases each (0.85%) as breast and thyroid carcinoma, one case 0.43(%) as seminoma and two cases (0.85%) as metastatic lesion; NOS.

In 113 cases of lymphadenopathy, the results obtained on FNAC were compared with the histopathological diagnosis of the corresponding excised lymph node. One hundred and three cases (91.15%) were true positives, six cases (6.78%) were false negatives and only four cases (4.52%) were false positives. Thus, a sensitivity of 94.49%, positive predictive value of 96.26%, and accuracy of 91.15% was observed.

### Discussion

Lymphadenopathy as a clinical manifestation of the regional or systemic disease serves as an excellent clue to the underlying disease. It can arise either from benign or malignant causes depending on the geographical condition and socioeconomic setup.<sup>[3]</sup> Cytology of lymph nodes has become a window for diagnosis of many diseases due to early availability of results, simplicity, and minimal trauma with less complication. FNAC has also been advocated as a useful method in comparison with more expensive surgical excision biopsies, especially in developing countries with limited financial and health care resources. Optimal material and experience, when combined, make cytological diagnosis of equal significance as histopathology. In many clinical settings, it is very difficult to decide which patient is more likely to have a reactive or neoplastic lymphadenopathy. Here, knowledge about the pattern of lymphadenopathy is helpful to the clinician for solving the dilemma.<sup>[4]</sup>

Lymph node lesions can be seen in patients ranging from very early to advanced age. In our study, the youngest patient with lymphadenopathy was a 4 months male infant and the oldest one was 78-year-old, with a mean age of 24.96 years. In our study, a male preponderance was noted with a male-to-female ratio of 1.2:1 which correlated with others.<sup>[5-7]</sup> In contrast, some other studies found a slight female predominance with a male to female ratio of 1:1.2.<sup>[8,9]</sup>

Cervical region was the most frequent site of lymphadenopathy in our study (75%) followed by

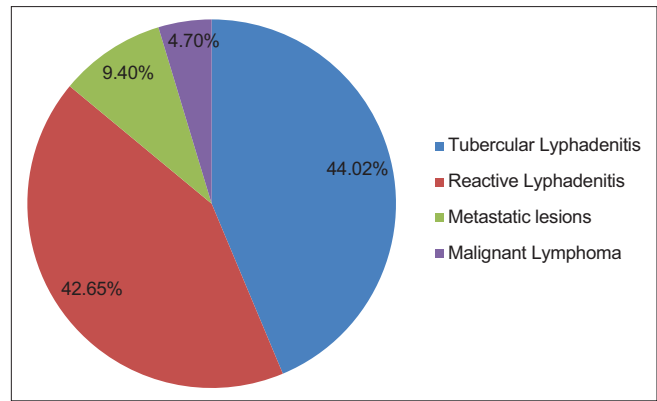


Figure 1: Percentage distribution of various lymph node lesions on fine needle aspiration cytology

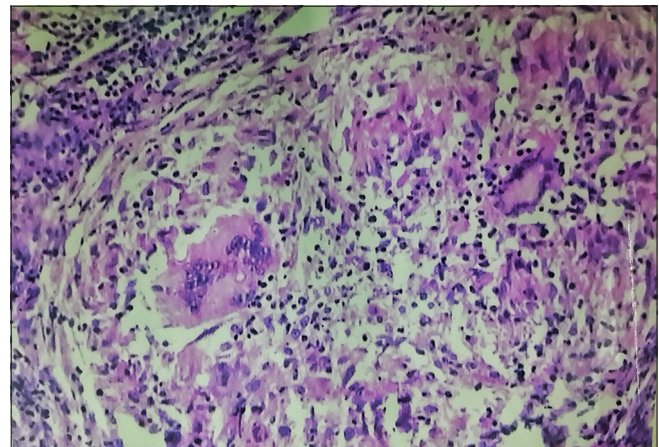


Figure 2: Granulomatous lymphadenitis (tuberculosis). Section showing Langhans giant cells (H and E, ×40)

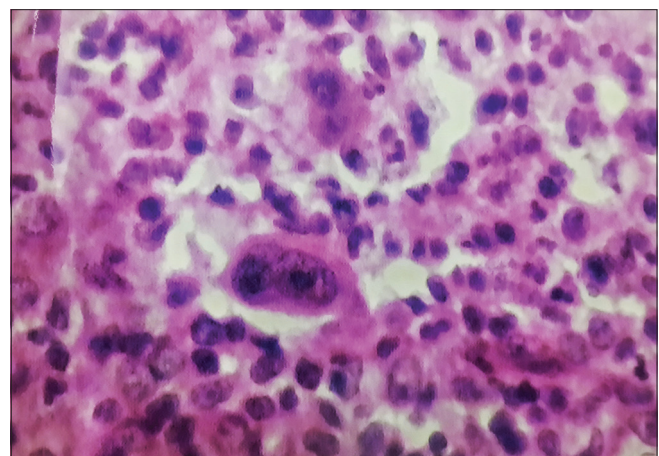


Figure 3: Hodgkin lymphoma. Section showing a binuclear Reed–Sternberg cell (H and E, ×40)

axillary (11.60%) and inguinal (6.70%). Cervical region was also seen as the most common site of involvement in other studies.<sup>[8,10,11]</sup> Collectively, benign disorders (86.34%) were more common than malignant disorders (13.67%) in the present study. This correlates well with other studies from India and other developing countries.<sup>[12-14]</sup> Tubercular

lymphadenitis (44.02%) was the most common cause of lymphadenopathy in our study followed by reactive lymphadenopathy (41.88%), metastatic deposits (9.40%), and malignant lymphoma (4.70%). Many other studies from India, Pakistan, and Sudan also found tuberculosis as the most common cause of lymphadenopathy.<sup>[8,9,14-16]</sup>

In the present study, a total of 22 patients (9.40%) had metastatic deposits in the lymph nodes. Adenocarcinoma (40.91%) was the most frequent metastatic lesion encountered, followed by squamous cell carcinoma (27.27%) and breast carcinoma (9.09%). Similar figures were seen in some studies<sup>[17,18]</sup> while a few other studies<sup>[7,15]</sup> found squamous cell carcinoma as the most common metastatic malignancy. Lymphomas constituted only 4.7% of lymphadenopathies in our study of which Hodgkin's lymphoma constituted 36.37% and NHL constituted 63.64% of cases, and this result was corroborated by other studies.<sup>[7,14]</sup> In contrast, a study from Egypt,<sup>[19,20]</sup> found that NHL (32.5%) contributed to most of the cases of lymphadenopathy followed by metastatic tumors (19.7%).

Overall, the sensitivity of 94.49%, positive predictive value of 96.26% and diagnostic accuracy of 91.15% was achieved in our study. In malignant conditions of lymph nodes, FNAC enjoys a high sensitivity and specificity, the average being 95%. The sensitivity and specificity of FNAC in metastatic tumors were reported to be 100% by many studies.<sup>[7,12]</sup>

To conclude, this study highlights the usefulness of FNAC as a simple, inexpensive, relatively painless, rapid, repeatable, and reliable method of investigation for lymphadenopathy, especially in OPDs, peripheral hospitals, and dispensaries, thus reducing the incidence of surgery and therefore, bed occupancy.<sup>[3]</sup> However, it is not a substitute for conventional surgical pathology but is complimentary to it.

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#### Conflicts of interest

There are no conflicts of interest.

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