

# Utility of Fine Needle Aspiration Cytology in Lymphadenopathy - A Study of 638 Cases in a Primary Care Setting

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## ABSTRACT

**Introduction:** In recent times, Fine Needle Aspiration Cytology (FNAC) has gained popularity as a screening and a diagnostic procedure. Many studies have been published elaborating its utility in patients of lymphadenopathy. Large numbers of them are from tertiary care centers. We have not come across any recent study from central Uttar Pradesh that details the utility of FNAC in profiling lymphadenopathy in a primary care setting.

**Aim:** To analyze various causes of lymphadenopathy in patients presenting at a primary care setting and to study their demographic profile, using FNAC as a diagnostic tool.

**Materials and Methods:** It is a retrospective study of

FNAC done on patients presenting with lymphadenopathy. Adequate material was obtained in 643 cases out of 660 patients on whom the procedure was performed over a period of over six years. Of these, 638 cases are further analyzed.

**Results:** Cervical lymph nodes were the commonest group to be involved in a disease process. Reactive lymphadenitis was the predominant lesion in children. In adults, tubercular lymphadenitis was seen most frequently. Metastatic involvement was the foremost lesion in geriatric patients.

**Conclusion:** FNAC is a useful preliminary diagnostic procedure in patients presenting with lymphadenopathy. Significant economic benefits can result if this technique is used more commonly in a primary care setting.

**Keywords:** Lymphadenitis, Lymph node cytology, Lymph node lesions

## INTRODUCTION

Lymphadenopathy is often a presenting or a dominant clinical manifestation in several disease processes. In our country, an accurate, early and timely accessibility as to the cause of lymphadenopathy is of considerable importance due to high prevalence of acute and chronic infective disorders and rapidly increasing incidence of neoplastic diseases. Earlier, to ascertain the cause of lymphadenopathy, biopsy of lymph node was the usual recourse available. This was feasible without much difficulty for superficial lymph nodes only. In recent times, employing Fine Needle Aspiration Cytology (FNAC) and radiological guidance, deep-seated lymph nodes too have become accessible for evaluation.

FNAC was first utilized in clinical medicine in early decades of twentieth century; however its status as a reasonably reliable diagnostic tool became established during last 30 to 40 years [1]. The procedure is all the more valuable in resource-poor economies like ours, because of its simplicity, low cost of operation and early availability of results [2]. Therefore the catchy acronym SAFE (Simple, Accurate, Fast and

Economical) coined by DeMay appears to be appropriate. However, scepticism still persists whether FNAC can replace biopsy as a diagnostic modality in routine clinical practice. In case of lymphadenopathy, it is advocated that patients with reactive lymph node enlargement or metastasis from a known malignancy can be spared lymph node excision. Conversely, patients with indeterminate cytology or a diagnosis of lymphoma should undergo mandatory surgical excision [1].

In this study, we present our experience of FNAC as a preliminary diagnostic procedure in a primary care setting for patients with lymphadenopathy. Our aim is to study the utility of FNAC in delineating various causes of lymphadenopathy, provide statistical data and document their demographic profile. Since selection bias is comparatively less in a primary care setting, we presume that our data will be a balanced evaluation of lymphadenopathy in this part of the country.

## MATERIALS AND METHODS

The present study is a retrospective analysis of FNAC carried

out for diagnostic purposes in Pathology section of Ama Diagnostic Centre Lucknow in collaboration with Department of Pathology Mayo Institute of Medical Sciences. The period of study is from August 2008 to October 2014. Only those patients, in whom a history incorporating basic clinical data along with characteristics of the lymph node group involved was available, were included. FNAC procedure was carried out using a 10 ml syringe equipped with 21 or 23 gauge needle. Depending on the quantum of aspirate obtained, a total of 3 - 6 air-dried and/or wet-fixed smears were prepared. May Grunwald Giemsa (MGG) and Papanicolaou staining technique was used. After initial evaluation of smears, if indicated, Zeihl Neelsen staining for acid fast bacteria and gram staining were also done. After studying the cytomorphological details, individual cases were classified into following group of disorders, based on criteria described in standard textbooks of cytology.

- 1.Reactive lymphadenitis
- 2.Tubercular lymphadenitis
- 3.Granulomatous lymphadenitis, suspicious of tuberculosis.
- 4.Supplicative lymphadenitis.
- 5.Primary lymphoproliferative disorders
- 6.Aspirates showing metastatic deposits

Patients of each specific disorder are further sub-classified into

**Group 1:** Paediatric patients - Age group less than 18 years

**Group 2:** Adult patients - Age group 18 to 59 years.

**Group 3:** Geriatric patients - Age group more than 60 years

When clinical features were supportive, cases showing only epithelioid cells/ epithelioid cell granulomas, without caseous necrosis or AFB positivity, were categorized as: 'granulomatous lymphadenitis, suspicious for tuberculosis'. Due to high prevalence of this disease in our country, such patients – many of whom cannot afford to undergo more extensive and expensive investigations for a definitive diagnosis of tuberculosis - are often given a therapeutic trial of anti-tubercular drugs. Cases with cytological diagnosis of 'suspicious of lymphoproliferative disorder' are included in the study only when a follow-up biopsy was available for confirmation.

## RESULTS

During the period - August 2008 to October 2014 - 660 patients of lymphadenopathy underwent fine needle aspiration procedure. Adequate material was obtained in 643 patients. Of these 643 patients, one case was of filarial lymphadenitis and in four cases no diagnosis could be rendered. They are excluded from further analysis. Of the

remaining 638 patients, 348 patients (54.5%) were male and 290 patients (45.5%) were female.

Distribution of different lymph node groups from which FNAC was done is shown in [Table/Fig-1]. It is seen that cervical lymph nodes are the commonest group to be involved by a disease process.

The disease and the sex-distribution of patients are shown in [Table/Fig-2]. It is observed that non-specific reactive lymphadenitis was the commonest diagnosis rendered (45.92% of all cases), followed by a diagnosis of tubercular lymphadenitis (22.1% of all cases). A diagnosis of 'granulomatous lymphadenitis, suspicious of tuberculosis' was given in 10.97% of all cases. If this group is also included within the ambit of mycobacteriosis, (because clinically, in our setup, majority would be treated as such), then mycobacterial lymphadenitis was seen in 33.0% of cases.

Analysis of sex distribution shows that reactive lymphadenitis is more common in males, tubercular involvement is slightly

Lymph Node Group Involved	Number of Patients	Percentage (%)
Cervical	543	85.1
Inguinal	44	6.9
Axillary	38	5.95
Abdominal	11	1.72
Others	02	0.30
Total number of cases	638	100

**[Table/Fig-1]:** Distribution of patients in relation to lymph node group involved.

Disease Category	Total Number of Patients (%age)*	Males (%age)†	Females (%age)‡
Tubercular lymphadenitis	141 (22.1)	67 (47.5%)	74 (52.5%)
Granulomatous lymphadenitis, suspicious of TB	70 (10.97)	32 (45.7%)	38 (54.3%)
Reactive lymphadenitis	293 (45.92)	163 (55.6%)	130 (44.4%)
Suppurative	49 (7.68)	27 (55.1%)	22 (44.9%)
Metastatic malignancy	66 (10.34)	44 (66.7%)	22 (33.3%)
Primary malignancy	19 (2.97)	15 (78.9%)	04 (21.1%)
Total number of patients	638 (100)	348	290

**[Table/Fig-2]:** The disease and sex-distribution of patients.

\* Percentage is in reference to total number of patients included in the present study. † Percentage is in reference to total number of patients of that particular disease ‡ Percentage is in reference to total number of patients of that particular disease

Cytological Diagnosis	Total number of patients	Group 1 (0-18 yrs)	Group 2 (19-59 yrs)	Group 3 (> 60 yrs)
Tubercular lymphadenitis	141	53 (37.6)	85 (60.3)	03 (2.1)
Granulomatous lymphadenitis suspicious of TB	70	27 (38.6)	42 (60)	01 (1.4)
Reactive lymphadenitis	293	156 (53.3)	128 (43.6)	09 (3.1)
Suppurative	49	09 (18.4)	36 (73.5)	04 (8.1)
Metastatic	66	02 (3.03)	40 (60.6)	24 (36.4)
Primary malignancy	19	04 (21)	12 (63.15)	03 (15.8)
Total number of patients	638	251	343	44

**[Table/Fig-3]:** Distribution in reference to age and the disease category of the patient.

\* Figure in parenthesis indicates percentage of patients in reference to total number of patients of that particular disease.

more frequent in females, and males are distinctly more often involved by a neoplastic process.

[Table/Fig-3] shows, distribution of patients with reference to their age and the disease category. In our study, reactive lymphadenitis is seen more often in group 1 patients. Tubercular lymphadenitis, suppurative lesions, metastatic infiltration and primary malignancies are more common in group 2 patients.

## DISCUSSION

In the present era of modern medicine, Dr. Grieg and Dr. Gray were probably the first to have utilized FNAC - for demonstration of trypanosomes in a lymph node aspirate [1]. In 1916, using FNAC, Dr. Aravandinos diagnosed splenic leishmaniasis [3]. Although, Dr. Martin and Dr. Ellis published their experience of FNAC in 662 cases of lymphadenopathy in 1930, the technique got its due recognition only after extensive work of researchers like Franzen et al., and Zajicek et al., from 1960 onwards, established its utility as an investigative procedure [4]. Unique selling points of FNAC, as published by several workers include - feasibility of carrying out the procedure in remote areas, rapid availability of results, high sensitivity and specificity, freedom from surgical procedure, low economic burden to the patient, absence of scar formation and minimal skill requirement for performing the procedure [2,5]. However, the question of interpretational skills required has not been addressed adequately in our country. This issue can only be resolved by carrying out double blind controlled studies of inter-observer variation in rendering a correct diagnosis.

In our series, lymph nodes of the head and neck region were

the dominant group to be involved by a disease process. As shown in [Table/Fig-4], these findings are similar to the observation of some other workers like Ahmad et al., [5], Egea et al., [6], Khajuria et al., [7], Hirachand et al., [8], Qadri et al., [9] and Srivastava et al., [10].

More frequent involvement of cervical lymph nodes in disease process is possibly due to their proximity to anatomical passages of the body that is constantly exposed to environmental infectious agents. Cervical lymph nodes also drain lymphatics of a very large part of the body, including those of head and neck, thorax and some abdominal organs. Likelihood of their involvement by metastatic processes is thus correspondingly high.

In our series, reactive lymphadenitis was responsible for maximum number of patients seeking clinical attention and it was seen more often seen in group 1 cases. Patients of this age group are more likely to be exposed to environmental infectious agents. Also parents tend to seek early medical opinion for their affected child. As shown in table 5, these findings are similar to those of Ahmad et al., [5], Hirachand et al., [8] and Qadri et al., [9] but at variance to those of Khajuria et al., [7] and Srivastava et al., [10].

In our study, tubercular lymphadenitis was the second most common cytological diagnosis. As shown in [Table/Fig-5], our findings are similar to those reported by Ahmad et al., [5] Hirachand et al., [8] and Qadri et al., [9] but at variance to those of Khajuria et al., [7] and Srivastava et al., [10].

Data from our series, as well as from many other studies [5,7,9], indicates that mycobacteriosis tends to involve the cervical lymph nodes most frequently. In our series, a group

Lymph node group	Present study	Srivastava et al., [10]	Qadri et al., [9]	Hirachand et al., [8]	Khajuria et al., [7]	Ahmad et al., [5]	Egea et al., [6]
Neck	85.1	90.04	76	75.3	80.3	73.6	67.5
Inguinal	6.9	3.48	06	9.23	3.11	6.0	09.0
Axillary	5.95	2.78	15.7	15.38	7.89	10.8	6.5

**[Table/Fig-4]:** Comparison of lymph node groups involved in different series\*.

\*All figures are in percentage

Diagnostic group	Present study	Ahmad et al., [5]	Khajuria et al., [7]	Hirachand et al., [8]	Qadri et al., [9]	Srivastava et al., [10]
Tubercular lymphadenitis	22.1	32.8	52.3	28	9.1	39.33
Granulomatous lymphadenitis suspicious of TB	10.97	-	-	9.2	-	4.1
Reactive lymphadenitis	45.92	53.6	37.2	41.5	36.9	34.93
Suppurative	7.68	-	1.0	3.0	4.5	4.5
Metastatic	10.34	9.1	3.8	12.3	38.2	11.5
Primary malignancy	2.97	4.5	3.0	6.0	8.5	2.25

**[Table/Fig-5]:** Comparison of disease distribution in different series.

of patients were diagnosed as 'granulomatous lymphadenitis suspicious of TB'. For the purpose of discussion, they are considered to fall under the diagnosis of tuberculosis. Although granulomatous lymphadenitis (GL) can be due to other causes like sarcoidosis, fungal infection, foreign body reactions and lymphomas, earlier studies from India indicate that most of these cases have tuberculosis as the underlying aetiology [11]. This is found to be true more often in children and young adults. Lymphoma can also show a cytological picture of granulomatous lymphadenitis [12]. Kumari et al., [12] caution that presence of exuberant granulomatous response in association with Hodgkin lymphoma or metastatic disease might distract the observer from the underlying pathology. As lymphoma occurs most often in older adults, it is our view that in this age group, if the clinical profile is not consistent with TB, GL should be investigated further - specifically by histological biopsy. Conversely, children and young adults can safely be given a therapeutic trial of ATT, if they show a cytological picture of GL.

In our series metastatic deposits in lymph nodes were seen in 10.34% of cases. This figure is similar to some other studies [5,7,10] but at variance to that of Qadri et al., [9]. The latter study was carried out at a referral centre; hence the variation is readily explained.

According to a WHO report, world over a total of 9.2 million new cases of tuberculosis were detected in 2008 [13]. Of these, India accounts for about 20% of cases. Thus the incidence of TB in India is around 1.84 million cases. In India, extrapulmonary TB (EPTB) constitutes 20% of all cases of TB in HIV negative individuals. According to the same report, nodal TB constitutes 35% of all cases of EPTB [14]. Extrapolation of this data indicates that about 0.12 million new cases of lymph node TB (LTB) occur every year in India.

If surgical biopsy alone was to be used for diagnosis of LTB, and assuming a conservative expenditure of \$100 being the cost of the procedure; the total outflow would be \$12.0 million/annum. FNAC procedure - cost if pegged at \$10.0

per case - will involve an expenditure of \$1.2 million only. If we extrapolate this data, to all patients presenting with LAP, much larger financial savings can be anticipated. Thus, use of FNAC as a primary diagnostic modality in patients of lymphadenopathy makes good economic sense in resource poor countries; even if the procedure is neither 100% specific nor 100% sensitive.

## LIMITATIONS

Although our study provides a balanced view of the profile of lymphadenopathy in general population, in a primary care setting, there are some limitations. Two important limitations are - absence of cyto-histological correlation and lack of follow-up data.

## CONCLUSION

FNAC is a useful preliminary diagnostic procedure in patients of lymphadenopathy presenting at a primary care setting. In our study, employing FNAC as a diagnostic procedure, it is seen that overall reactive lymphadenitis is the commonest cause of lymphadenopathy. More than half of the patients in group 1 have lymphadenitis of reactive nature. Tuberculosis, suppurative lesions, metastatic infiltration and primary malignancies are seen more often in adults, with tuberculosis being the dominant cause of lymphadenopathy in young adults. Routine use of FNAC as a diagnostic procedure can yield significant economic benefit for the nation.

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