



## “Incidence of Tuberculosis among cases of peripheral lymphadenopathies and techniques useful in the diagnosis of Tuberculous lymphadenitis by FNAC – Our experience from a tertiary health care centre”

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**ABSTRACT** **INTRODUCTION:** Tuberculosis is an important cause of morbidity and mortality in developing countries. Tuberculous lymphadenitis is the most common form of extrapulmonary Tuberculosis. Proper diagnosis and prompt treatment of Tuberculosis is very important. This study will emphasize the role of FNAC in the diagnosis of Tuberculous lymphadenitis and the importance of techniques like AFB staining and CBNAAT in diagnosing equivocal cases

**OBJECTIVES:** To study the incidence of tuberculosis among the cases of peripheral lymphadenopathy, to study the various cyto-morphological patterns of tuberculous lymphadenitis and to emphasize the importance of AFB staining & CBNAAT in the correct diagnosis of tuberculosis.

**MATERIALS AND METHODS:** A retrospective study is carried out for a period of one year. FNAC was done for 547 patients with peripheral lymphadenopathy. The cyto-morphological pattern of these cases are presented along with AFB positivity and detection of Mycobacterium Tuberculosis by CBNAAT.

**RESULTS:** Out of 547 patients with superficial lymphadenopathy, 177 cases were diagnosed as Tuberculous lymphadenitis. The ratio of males to females was 1: 1.5. There were maximum number of cases in the age group of 31- 40 years. Among the cases of Tuberculosis, there were 29 cases of granuloma without necrosis, 99 cases of granuloma with caseation necrosis, 18 cases of caseation without granuloma and 29 cases of caseation with abscess without granuloma. Overall 76 (42.9%) cases were positive for AFB. CBNAAT was positive in 18 cases.

**CONCLUSION:** Fine needle aspiration cytology (FNAC) is a safe and simple investigation used to diagnose Tuberculous lymphadenitis. Demonstration of the presence of Acid fast bacilli by Fluorescence microscopy, Zeihl-Neelsen staining and the CBNAAT improves the sensitivity and specificity of FNAC.

### KEYWORDS :

#### Introduction

Tuberculosis, one of the most ancient disease of the mankind, still remains a major public health challenge. In spite of the newer techniques for diagnosis and treatment of Tuberculosis, unfortunately, millions of people are suffering from this disease worldwide. India accounts for one fourth of the global TB burden.<sup>1</sup>

There are numerous causes of peripheral lymphadenopathy. This list includes reactive lymphadenitis (secondary to viral and bacterial infections), Tuberculosis, lymphomas, sarcoidosis, metastatic malignancies and uncommon causes like fungal diseases, toxoplasmosis and diseases of the mononuclear phagocyte system among others.<sup>2</sup> In India, Tuberculous lymphadenitis remains one of the most common causes of lymphadenitis.

Fine needle aspiration cytology (FNAC) is the widely practised investigation in the evaluation of lymphadenopathies. It is a safe, simple, rapid and cost-effective procedure used as a first line investigation in cases of lymphadenopathy. The aspirated material is stained and studied for the presence of granulomas and caseous necrosis. In some late cases of Tuberculous lymphadenitis, there is liquefaction and abscess formation. In these cases it is difficult to find the usual diagnostic cytological findings like epithelioid granuloma and caseous necrosis. The use of additional techniques like demonstration of the presence of Acid fast bacilli in the aspirate by Fluorescence microscopy, Zeihl-Neelsen staining and culture has been practised widely to improve the sensitivity and specificity of the Fine needle aspiration technique. These additional tests are especially useful in cases presenting as suppurative lesions which may be missed by cytomorphological study alone.

The CBNAAT – MTB/RIF by Xpert MTB/RIF assay is a new test that is revolutionizing tuberculosis (TB) control by contributing to the rapid diagnosis of TB disease and drug resistance. It is based on Cartridge based nucleic acid amplification. The test simultaneously detects Mycobacterium tuberculosis and resistance to rifampicin (RIF) in less than 2 hours. In comparison, standard cultures can take 2 to 6 weeks for MTBC to grow and conventional drug resistance tests can add 3 more weeks. The information provided by the Xpert MTB/RIF assay aids in selecting treatment regimens and reaching infection control decisions quickly.<sup>3</sup>

The aim of the present study is

1. To study the incidence of tuberculosis among the cases of peripheral lymphadenopathy attending the FNAC laboratory of a tertiary care centre.
2. To study the various cyto-morphological patterns of tuberculous lymphadenitis.
3. To emphasize the importance of AFB staining & CBNAAT in the correct diagnosis of tuberculosis.

We report our experience of FNAC examination of 547 cases of peripheral lymphadenopathy over a period of 1 year.

#### Materials and Methods

The present retrospective study was undertaken at the cytopathology lab of Mahatma Gandhi Memorial Government Hospital, attached to the KAPV Government Medical College, Trichy. The study was started after obtaining approval from the Institutional Ethical Committee.

The study material was taken from 547 patients referred to the cytopathology lab for FNAC of lymph nodes over a period of 1 year from July 15 to June 16. Informed consent was obtained from all the patients. After clinical examination, under strict aseptic precautions, FNAC was performed using 5ml disposable syringe with 23G or 22G needle. Smears were made from the aspirated material, fixed in 95% Isopropyl alcohol and stained with Haematoxylin & Eosin stain. Additional air dried smears were made and stained with Auramine O stain and Zeihl-Neelsen stain for Acid fast bacilli. In selected cases with purulent aspirates, the material was sent to Microbiology department for CBNAAT - MTB/RIF by Xpert MTB/RIF - CEPHIED.

The cytological diagnoses were analysed to find out the incidence of Tuberculosis and other pathological conditions among the cases of superficial lymphadenopathies. The patients diagnosed as reactive lymphadenitis were followed up and reviewed after 4 weeks. Repeat FNAC was performed if there was persistent lymph node enlargement. The cases of Tuberculous lymphadenitis were further analysed for the various cyto-morphological patterns of presentation.

#### Results

Among the 547 cases of lymphadenopathy, there were 216 cases of nonspecific reactive lymphadenopathy, 177 cases of Tuberculous

lymphadenitis, 99 cases of Metastatic Carcinoma, 34 cases of nonspecific suppurative lymphadenitis, 11 cases of lymphoproliferative disorders, 8 cases of undifferentiated malignancy, 1 case of Kikuchi necrotizing lymphadenitis and 1 case of leukemic infiltration. Table – 1 shows the different cytological diagnoses made by FNAC.

**Table – 1.**

Diagnosis	No. of cases	Percentage
Nonspecific Reactive lymphadenitis	216	39.5%
Tuberculous Lymphadenitis	177	32.4%
Metastatic Carcinoma	99	18.1%
Suppurative lymphadenitis	34	6.2%
Lympho proliferative disorder	11	2.0%
Undifferentiated Malignancies	08	1.5%
Others	02	0.03%

The age and sex distribution of cases of Tuberculous lymphadenitis was analysed and tabulated. (Table -2). There were more cases of females compared to males. The ratio of males to females was 1: 1.5. There were maximum number of cases in the age group of 31- 40 years followed by 21-30 years and 11-20 year age groups. The incidence was declining after the age of 40 years.

**Table - 2**

Age group (Years)	Males	Females	Total	Percentage
0-10	03	06	09	5.1%
11-20	11	28	39	22.0%
21-30	14	29	43	24.3%
31-40	19	25	44	24.8%
41-50	17	10	27	15.3%
51-60	04	02	06	3.4%
More than 60	04	05	09	5.1%
Total	72	105	177	

The sites of lymph node involvement in the cases of Tuberculous lymphadenitis were analysed. Cervical nodes were the most commonly involved group with frequent occurrence of multiple and matted nodes. Axillary nodes were the next common group of nodes affected.

The cyto-morphological patterns of the cases of Tuberculous lymphadenitis were studied. There were 29 cases of granuloma without necrosis, 99 cases of granuloma with caseation necrosis, 18 cases of caseation without granuloma and 29 cases of caseation with abscess without granuloma.

For all the cases, additional smears were made and studied for AFB by Auramine fluorescence microscopy and Zeihl-Neelsen staining. The various cyto-morphological patterns and the corresponding AFB positivity is given in Table - 3.

**Table - 3**

Cytologic Pattern	No. of cases (%)	AFB positive cases (%)
Granuloma without necrosis	29 (16.4%)	1 (3.4%)
Granuloma with caseation necrosis	99 (55.9%)	46 (45.5%)
Caseation necrosis without granuloma	18 (10.2%)	9 (50%)
Abscess without granuloma	31 (17.5%)	20 (64.5%)
Total	177	76 (42.9%)

Cartridge based Nucleic Acid Amplification Test (CBNAAT) – MTB/RIF using the Xpert MTB/RIF – CEPHIED was done for 30 cases of purulent aspirates. Among these Mycobacterium tuberculosis was detected in 18 cases and rifampicin resistance was detected in two of the cases. Two cases of tuberculosis with caseating granuloma and abscess were negative for MTB by CBNAAT. Nine cases presenting with abscess were negative for AFB but MTB was detected by CBNAAT.

## Discussion

Tuberculous lymphadenitis is the most common presentation of extrapulmonary Tuberculosis. Early diagnosis of Tuberculous lymphadenitis by the simple FNAC test and starting anti-tuberculous treatment plays a very important role in control of the disease.

In our study, majority of cases of peripheral lymphadenopathy were

diagnosed as reactive lymphadenitis (39.5%) followed by Tuberculous lymphadenitis (32.4%). Malignancies constitute 21.6% cases. Mohan A et al. in their study have found similar trend with 35.6% of reactive lymphadenitis, 31.3% of tuberculous lymphadenitis and 25.9% of malignancies.<sup>2</sup>

In our study, the male to female ratio for Tuberculous lymphadenitis was 1:1.5. Saurabh Kumar Singh et al.<sup>4</sup> and Fontanilla *et al.*,<sup>5</sup> in their study had found a similar ratio of 1:1.4. In our study majority of patients were in the age group of 21-40 years (49.1%).

Cervical lymph node involvement was the most common presentation of lymph nodal tuberculosis in our study.

The most common cytological pattern noted in our study was epithelioid granuloma with caseous necrosis (55.9%) followed by abscess without granuloma (17.5%). Study by Handa *et al.* reported a combination of epithelioid cell granulomas and caseous necrosis in 34% cases, epithelioid cell granulomas without caseous necrosis in 12% cases, and only caseous necrosis unassociated with granulomas in 26% cases.<sup>6</sup>

The overall AFB positivity in our study was 42.9% and the highest percentage of AFB positivity was noted in cases of cold abscess without granuloma (64.5%). The highest percentage of AFB positivity (64.7%) was also observed in aspirate containing purulent/pus and caseous/cheesy material by Priyanka Chand *et al.*<sup>7</sup>

The introduction of nucleic acid amplification (NAA) testing into TB testing algorithms has brought the promise of accurate and time efficient methods for detecting Mycobacterium tuberculosis bacteria and mutations associated with drug resistance.

In our study Cartridge based Nucleic Acid Amplification Test (CBNAAT) – MTB/RIF using the Xpert MTB/RIF – CEPHIED was done for 30 cases of purulent aspirates and Mycobacterium tuberculosis was detected in 18 cases. Rifampicin resistance was detected in two of the cases.

In Nine cases presenting with abscess without granuloma and negative for AFB, MTB was detected by CBNAAT. The diagnosis of these cases would have been missed if CBNAAT was not done. Recently, WHO recommends GeneXpert to be used as one of the initial diagnostic test in patients suspected of having extra-pulmonary tuberculosis, including lymph node tuberculosis.<sup>8</sup> This CBNAAT test could have the potential to improve the diagnosis of TB in those that are likely to be missed by traditional tests.<sup>9</sup>

## Conclusion

Tuberculous lymphadenitis is the most common form of extrapulmonary Tuberculosis. Fine needle aspiration cytology (FNAC) is a safe and simple investigation used to diagnose Tuberculous lymphadenitis. The aspirate can also be used for demonstration of the presence of Acid fast bacilli by Fluorescence microscopy, Zeihl-Neelsen staining and the CBNAAT – MTB/RIF which improve the sensitivity and specificity of FNAC.

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