Original Research

PROSPECTIVE COMPARISON OF CBNAAT, FINE NEEDLE ASPIRATION CYTOLOGY, AND HISTOPATHOLOGICAL EXAMINATION FOR THE DIAGNOSIS OF SUSPECTED TUBERCERCULAR LYMPHADENOPATHY

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ABSTRACT

Background: Tuberculous lymphadenopathy is the most common form of extra-pulmonary tuberculosis and poses a significant diagnostic challenge. Early and accurate diagnosis is essential for timely treatment. This study was conducted to compare the diagnostic utility of Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) with Fine Needle Aspiration Cytology (FNAC) and Histopathological Examination (HPE) in suspected palpable tuberculous lymphadenopathy.

Methodology: A prospective comparative study was conducted in the Department of Pathology in collaboration with the Department of General Surgery at Sree Mookambika Institute of Medical Sciences, Kulasekharam, from July 2025 to January 2026. Fifty patients with suspected palpable tuberculous lymphadenopathy were enrolled. Following clinical evaluation and baseline investigations, FNAC was performed in all cases. Subsequently, excisional lymph node biopsy was carried out and specimens were subjected to CBNAAT and histopathological examination. Histopathology was considered the reference standard. Statistical analysis was performed using Epi Info software.

Results: Histopathology diagnosed tuberculosis in 60% of cases, FNAC in 58%, and CBNAAT detected Mycobacterium tuberculosis in 46% of cases. FNAC demonstrated a sensitivity of 93.1%, specificity of 85.7%, positive predictive value of 90%, and negative predictive value of 90%. CBNAAT showed a sensitivity of 100%, specificity of 74.07%, positive predictive value of 66.66%, and negative predictive value of 100%. Rifampicin resistance was detected in 10% of microbiologically confirmed cases.

Conclusion: FNAC is an effective initial diagnostic tool, while CBNAAT provides rapid microbiological confirmation and detection of rifampicin resistance. Combined use of FNAC, CBNAAT, and histopathology improves the diagnostic accuracy of tuberculous lymphadenopathy.

Keywords: Tuberculous Lymphadenopathy, CBNAAT, FNAC, Histopathology, Extra-Pulmonary Tuberculosis, Rifampicin Resistance.

INTRODUCTION

Tuberculosis (TB) remains one of the leading infectious causes of morbidity and mortality worldwide. According to the World Health Organization (WHO), approximately 10 million people developed TB and 1.4 million deaths were attributed to the disease globally. India bears the highest burden of tuberculosis, accounting for nearly 21% of the global incidence. Despite substantial advances in diagnosis and treatment, TB continues to pose a major public health challenge, particularly in developing countries.

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Extra-pulmonary tuberculosis (EPTB) constitutes a significant proportion of the total TB burden. It accounts for approximately 10–50% of TB cases in human immunodeficiency virus (HIV)-negative individuals and 35–80% among HIV-infected patients. Tuberculous lymphadenitis is the most common form of EPTB, representing nearly 40% of all extra-pulmonary cases and approximately 15–20% of all tuberculosis cases reported in India. It is more frequently observed in children, females, and immunocompromised individuals, particularly those with HIV infection.

Tuberculous lymphadenitis is a chronic granulomatous inflammatory disease of lymph nodes caused by infection with Mycobacterium tuberculosis. The cervical lymph nodes are most commonly involved, followed by mediastinal, supraclavicular, mesenteric, axillary, and inguinal lymph nodes. Clinically, patients usually present

with a slowly enlarging, painless swelling of one or more lymph nodes, often persisting for several weeks to months. Although clinical features and radiological findings may suggest a tuberculous etiology, they are insufficient for establishing a definitive diagnosis.

The confirmation of tuberculosis requires demonstration of the causative bacilli from the affected tissue. Conventional diagnostic methods include Ziehl–Neelsen (ZN) staining, mycobacterial culture, fine needle aspiration cytology (FNAC), and histopathological examination (HPE). However, acid-fast bacilli (AFB) can be demonstrated in only 25–30% of cases with tuberculous granulomas, limiting the sensitivity of direct smear microscopy. Although culture remains the gold standard for diagnosis, its utility is restricted by the prolonged turnaround time of 4–6 weeks. Histopathological examination of lymph node tissue can demonstrate characteristic features such as granulomatous inflammation with caseous necrosis and may aid diagnosis when combined with microbiological methods.

Fine needle aspiration cytology has emerged as a rapid, minimally invasive, and cost-effective technique for the initial evaluation of lymphadenopathy. However, its diagnostic accuracy may be limited by low specificity and inability to provide microbiological confirmation in some cases. Recent advances in molecular diagnostics have led to the development of Cartridge-Based Nucleic Acid Amplification Test (CBNAAT), which enables rapid detection of Mycobacterium tuberculosis DNA and identification of rifampicin resistance within a few hours. CBNAAT has shown promising sensitivity and specificity in both pulmonary and extra-pulmonary TB and has been endorsed by national and international guidelines.

Aim

To compare the diagnostic efficacy of Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) with Fine Needle Aspiration Cytology (FNAC) and Histopathological Examination (HPE) in patients presenting with suspected palpable tuberculous lymphadenopathy.

Objectives

1. To evaluate the diagnostic performance of CBNAAT in patients with suspected palpable tuberculous lymphadenopathy.
2. To compare the diagnostic yield of CBNAAT with Fine Needle Aspiration Cytology (FNAC).
3. To compare the diagnostic accuracy of CBNAAT with Histopathological Examination (HPE) of lymph node tissue.

MATERIALS AND METHODS

This prospective comparative study was conducted in the Department of Pathology in collaboration with the Department of General Surgery at Sree Mookambika Institute of Medical Sciences, Kulasekharam, Tamil Nadu, from July 2025 to January 2026. Prior approval was obtained from the Institutional Ethics Committee before commencement of the study. Written informed consent was obtained from all study participants. Patients presenting with clinically suspected palpable tuberculous lymphadenopathy and fulfilling the inclusion and exclusion criteria were enrolled consecutively during the study period.

A detailed clinical history was obtained, and a structured questionnaire was administered to all participants. Each patient underwent a thorough general physical examination and baseline laboratory investigations, including complete blood count (CBC), erythrocyte sedimentation rate (ESR), bleeding time (BT), clotting time (CT), random blood sugar (RBS), renal function tests (RFT), liver function tests (LFT), HIV serology, hepatitis B surface antigen (HBsAg), chest radiography, and Mantoux test.

Patients with suspected tuberculous lymphadenopathy were subjected to fine needle aspiration cytology (FNAC) after obtaining informed consent, and the aspirated material was sent to the Department of Pathology for cytological evaluation. Subsequently, irrespective of the FNAC findings, all patients underwent excisional lymph node biopsy. The excised lymph node specimen was divided into two portions. One portion was crushed under aseptic precautions and transported in a sterile falcon tube containing normal saline for Cartridge-Based Nucleic Acid Amplification Test (CBNAAT). The second portion was preserved in 10% buffered formalin and submitted for histopathological examination (HPE).

Histopathological findings were considered the reference standard for diagnosis. The results obtained from CBNAAT and FNAC were compared with histopathological findings to evaluate their diagnostic performance.

Statistical analysis was performed using Epi Info software developed by the Centers for Disease Control and Prevention (CDC), Atlanta, USA. Descriptive statistics were used to summarize demographic and clinical characteristics. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of CBNAAT and FNAC were calculated using histopathological examination as the gold standard. Agreement between the diagnostic modalities was assessed, and a p-value of less than 0.05 was considered statistically significant.

RESULT

Most of the patients were belong to 21 – 40 yr age group (40%) with mean age of study population was 29±15.64 yrs. The male and female patient having equal contribution (50%) in this study. Most of the patients (60%) were from rural areas.Mean BMI of study population was 44±13.75kg/m^2. Most of the cases (84%) were belong to lower socioeconomic class.

Table 1: Sociodemography

Age (yrs)	Number	Percentage
Up to 20	18	36
21 – 40	23	46
41 – 60	5	10
61 – 80	4	8
Residence		
Rural	30	60
Urban	20	40
BMI		
<18.5	13	26.0
18.5 – 24.99	17	34.0
25.0 – 29.9	15	30.0
≥ 30	5	10.0
Socio-Economic-Class		
(V) Lower class	25	50
(IV) Lower middle class	17	34
(III) Middle class	5	10
(II) Upper middle class	3	6
(I) Upper class	0	0
41 – 60	5	10

Only 30% of the patients having history of contact with TB case, 8% of the patients had past history of TB and 18% of the patients had positive family history of TB. Most common presenting complain was swelling (100%) followed by loss of weight (50%) and loss of appetite (40%).

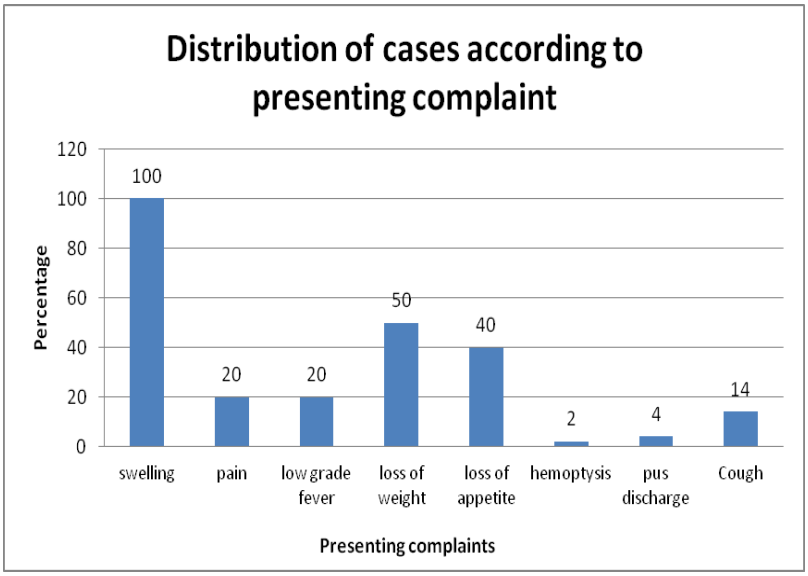


Figure 1: Presenting Complaints Most of the Patients (80%) Were Presented with Cervical Lymphadenopathy Followed by Axillary (10%), Inguinal (4%), Submandibular (4%) and Supraclavicular Lymphadenopathy (2%). Most of the Patientspresented with Firm Lymph Nodes (88%) Followed Bymatted (60%) and Fluctuation (10%) Whereas Only 2% of the Cases Had Sinus

Table 2: Site and Clinical Nature of Presenting Lymph Nodes

Site of lymphadenopathy	Number	Percentage
Cervical	40	80
Axillary	5	10
Inguinal	2	4
Submandibular	2	4
Supraclavicular	1	2
Clinical feature		
Firm	44	88.0
Fluctuation	5	10.0
Sinus	1	2.0
Matted	30	60

54% of the patients had positive mantoux test for TB, Mean ESR was 43±24.01 per hr, 14% of the patients having parenchymal lesion suggestive of tuberculosis on their chest X ray. On histopathology, 60% cases were diagnosed as tuberculosis whereas 58% of the patientsdiagnosed as tubercular on FNAC and 46% of the patients were found to be microbiologically confirmed for mycobacterium tuberculosis on CBNAAT. In our study, 10% of the patients had microbiologically confirmed case on CBNAAT with rifampicin resistance. The refampicin resistance was found in 2 male and 3 female.

In our study, histopathology was taken as gold standard diagnostic modality. When compared histopathology to CBNAAT, the true positive were 23 whereas true negative were 20.So Positive Predictive Value = 66.66, Negative Predictive Value = 100, Sensitivity = 100%, and Specificity= 74.07% of CBNAAT. Difference between two groups were found to be statistically significant. ($p<0.05$)

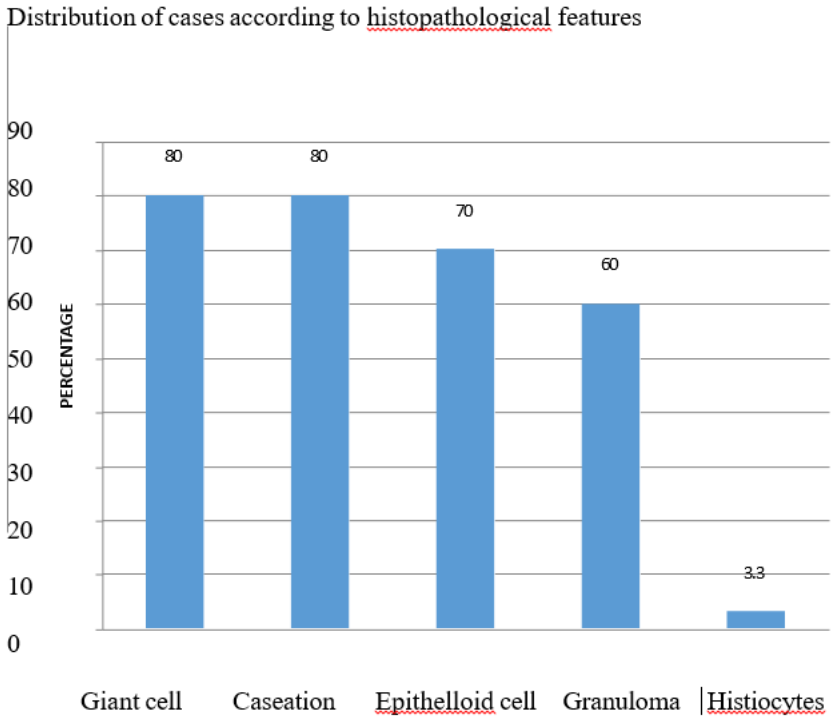
When compared histopathology to FNAC, the true positive were 27 whereas true negative were 18.So Positive Predictive Value = 90%, Negative Predictive Value = 90%, Sensitivity = 93.1%, and Specificity= 85.71% of FNAC. Difference between two groups were found to be statistically significant. ($p<0.05$).

Table 3: Comparision of Histopathology, FNAC and CBNAAT

Histopathology	CBNAAT		
	Positive	Negative	Pvalue
Positive	23	7	0.001*
Negative	0	20	
Total	23	27	
Histopathology	FNAC		
Positive	27	3	0.001*
Negative	2	18	
Total	29	21	

On histopathology, most of the patientshad giant cell and caseation (80%), followed by epitheloid cell (70%) whereas only 3.3% cases had histiocytes.

Figure 2: Histopathological findings



DISCUSSION

Tuberculous lymphadenitis is the most common form of extra-pulmonary tuberculosis and remains a significant diagnostic challenge, particularly in resource-limited settings. The present study compared the diagnostic utility of Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) with Fine Needle Aspiration Cytology (FNAC) and Histopathological Examination (HPE) in patients with suspected palpable tuberculous lymphadenopathy.

In the present study, the majority of patients belonged to the younger age group, with most cases occurring between 21 and 40 years of age. Similar findings have been reported by Sharma et al. and Fontanilla et al., who observed that tuberculous lymphadenitis predominantly affects young adults in economically productive age groups.[14,15] Most participants belonged to rural areas and lower socioeconomic classes, which may be attributed to overcrowding, poor nutrition, and limited access to healthcare facilities, factors known to increase the risk of tuberculosis.[16]

Clinically, all patients presented with lymph node swelling, making it the most common presenting complaint. Constitutional symptoms such as loss of weight and loss of appetite were observed in 50% and 40% of patients, respectively. These findings are consistent with previous studies that reported painless lymph node enlargement as the hallmark presentation of tuberculous lymphadenitis.[15,17] Cervical lymph node involvement was observed in 80% of cases, followed by axillary and inguinal lymphadenopathy. Similar predominance of cervical lymph node involvement has been documented in earlier studies, reflecting the common route of lymphatic spread of Mycobacterium tuberculosis.[18]

Mantoux test positivity was observed in 54% of cases, while chest radiography demonstrated pulmonary lesions suggestive of tuberculosis in only 14% of patients. These findings highlight the limited utility of these investigations in establishing a definitive diagnosis of tuberculous lymphadenitis, particularly in isolated extra-pulmonary disease.[19]

Histopathological examination diagnosed tuberculosis in 60% of cases and was considered the reference standard in the present study. The most common histopathological findings were caseous necrosis and Langhans giant cells, observed in 80% of positive cases, followed by epithelioid granulomas. Similar microscopic features have been consistently reported as characteristic findings in tuberculous lymphadenitis.[20]

FNAC diagnosed tuberculosis in 58% of cases and demonstrated a sensitivity of 93.1%, specificity of

85.7%, positive predictive value of 90%, and negative predictive value of 90% when compared with histopathology. These findings support previous studies that identified FNAC as a rapid, minimally invasive, and cost-effective initial diagnostic modality for tuberculous lymphadenitis.[21] However, FNAC may occasionally fail to distinguish tuberculosis from other granulomatous lesions, thereby limiting its specificity.

CBNAAT detected Mycobacterium tuberculosis in 46% of patients and identified rifampicin resistance in 10% of microbiologically confirmed cases. When compared with histopathology, CBNAAT demonstrated a sensitivity of 100%, specificity of 74.07%, positive predictive value of 66.66%, and negative predictive value of 100%. The excellent sensitivity and negative predictive value observed in the present study emphasize the usefulness of CBNAAT as a rapid molecular diagnostic tool capable of detecting both tuberculosis and rifampicin resistance within a short time frame.[22,23]

Overall, both FNAC and CBNAAT showed statistically significant agreement with histopathological findings ($p<0.05$). While FNAC exhibited higher specificity, CBNAAT provided rapid microbiological confirmation and drug-resistance detection. Therefore, CBNAAT should be used as a complementary diagnostic modality alongside FNAC and histopathology for early and accurate diagnosis of tuberculous lymphadenopathy.

CONCLUSION

The present study demonstrated that both Fine Needle Aspiration Cytology (FNAC) and Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) are valuable diagnostic modalities in the evaluation of suspected tuberculous lymphadenopathy. Histopathological examination remained the reference standard for diagnosis; however, FNAC showed high sensitivity (93.1%) and specificity (85.7%), making it an effective, minimally invasive, and cost-effective initial diagnostic tool.

CBNAAT exhibited excellent sensitivity (100%) and negative predictive value (100%), highlighting its usefulness in rapidly confirming tuberculosis and excluding disease when the test result is negative. An additional advantage of CBNAAT was its ability to detect rifampicin resistance, which was identified in 10% of microbiologically confirmed cases, thereby facilitating early recognition of drug-resistant tuberculosis and timely initiation of appropriate therapy.

The statistically significant correlation between FNAC, CBNAAT, and histopathological findings supports the complementary role of these diagnostic modalities. While FNAC provides rapid cytological assessment, CBNAAT offers microbiological confirmation and drug-resistance detection, enhancing diagnostic accuracy.

Therefore, the combined use of FNAC and CBNAAT along with histopathological examination can significantly improve the early diagnosis and management of tuberculous lymphadenopathy, particularly in high-burden settings. Early and accurate diagnosis may contribute to prompt treatment initiation, reduced morbidity, and better patient outcomes.

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