RESEARCH PAPER

Diagnostic Accuracy of Eosinophilic Bodies in Fine-Needle Aspiration Cytology of Tuberculous Lymphadenitis

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ABSTRACT

Background:

Extrapulmonary tuberculosis (EPTB), particularly tuberculous lymphadenitis, poses significant diagnostic challenges due to its paucibacillary nature and frequent smear-negative presentation. Eosinophilic bodies (EBs), identified in cytological smears, may serve as a useful adjunct diagnostic marker.

Aim:

To evaluate the diagnostic utility of eosinophilic bodies in fine-needle aspiration cytology (FNAC) smears of suspected tuberculous lymphadenitis, using CBNAAT as the reference standard.

Materials and Methods:

This prospective observational study was conducted at a tertiary care center from February 2024 to January 2025 and included 200 patients with clinically suspected tuberculous lymphadenitis. FNAC smears were stained using Leishman and Ziehl–Neelsen (ZN) methods. Parallel samples were analyzed by CBNAAT. Diagnostic parameters including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Results:

Eosinophilic bodies were detected in 175 cases (87.5%). CBNAAT confirmed tuberculosis in 190 cases (95%). The sensitivity of eosinophilic bodies was 92.1%, which was higher than that of AFB staining (78.9%), while both methods demonstrated 100% specificity and PPV. The negative predictive value of eosinophilic bodies (40%) was higher than that of AFB staining (20%). Eosinophilic bodies reduced false-negative cases (15 vs 40) and were frequently observed in cytological smears, particularly in necrotic aspirates. Cervical lymphadenopathy was the most common presentation (77%).

Conclusion:

Eosinophilic bodies are a reliable and cost-effective adjunct cytological marker that significantly improves diagnostic sensitivity in tuberculous lymphadenitis. Their incorporation into routine FNAC evaluation may enhance early diagnosis, particularly in smear-negative cases and resource-limited settings.

Keywords: Tuberculosis; Eosinophilic bodies; FNAC; CBNAAT; Lymphadenitis

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Introduction

Tuberculosis (TB) remains one of the leading infectious causes of morbidity and mortality worldwide, with a substantial burden in India. According to the World Health Organization Global Tuberculosis Report, India contributes nearly a quarter of global TB cases, reflecting the

continued public health challenge posed by the disease [1].

Extrapulmonary tuberculosis (EPTB) accounts for approximately 15–20% of all TB cases, with lymph node involvement being the most common manifestation [2]. Tuberculous lymphadenitis, particularly involving cervical lymph nodes, is frequently encountered in clinical practice. However, its diagnosis remains challenging due to the paucibacillary nature of the disease, absence of classical granulomas in certain cases, and a high proportion of smear-negative presentations [2,3].

Fine-needle aspiration cytology (FNAC) is widely used as a first-line diagnostic tool because of its simplicity, rapidity, and cost-effectiveness. It plays a crucial role in evaluating lymphadenopathy, particularly in resource-limited settings [3]. Classical cytological features such as epithelioid granulomas, Langhans giant cells, and caseous necrosis are considered suggestive of tuberculosis. However, these features may not always be present, especially in early disease or in immunocompromised patients, thereby reducing diagnostic sensitivity [3,4].

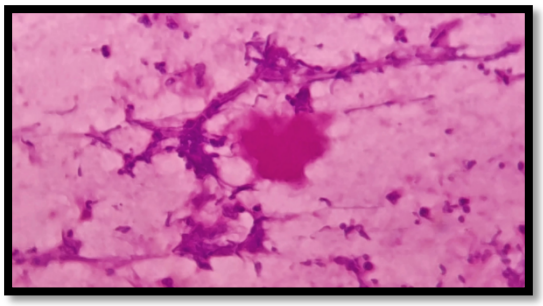
Conventional Ziehl–Neelsen (ZN) staining for acid-fast bacilli (AFB), although highly specific, has limited sensitivity in paucibacillary conditions [5]. In recent years, molecular diagnostic techniques such as CBNAAT (Xpert MTB/RIF) have revolutionized TB diagnosis by enabling rapid detection of *Mycobacterium tuberculosis* and rifampicin resistance within a short time frame [6,7]. Despite its high sensitivity and specificity, the availability of CBNAAT remains limited in many peripheral and resource-constrained healthcare settings [7].

Given these limitations, there is a growing need for additional cytomorphological markers that can improve diagnostic accuracy in tuberculous lymphadenitis. Eosinophilic bodies (EBs), described as amorphous, compact, extracellular aggregates of degenerated nuclear and cellular material which are sharply demarcated, eosinophilic and non refractile [Fig.1] are increasingly recognized in cytological smears of tuberculous lymphadenitis [8,9]. These structures are believed to be associated with necrotic processes and may serve as a useful morphological indicator, particularly in cases where granulomas are poorly formed or AFB is not demonstrable.

Previous studies have highlighted the role of adjunct cytological features in improving diagnostic yield in tuberculosis, especially in smear-negative cases [4,9]. However, the diagnostic significance of eosinophilic bodies remains underexplored and is often overlooked in routine cytological evaluation.

Therefore, the present study aims to evaluate the diagnostic utility of eosinophilic bodies in FNAC smears of tuberculous lymphadenitis, using CBNAAT as the reference standard, and to assess their potential role as a cost-effective adjunct marker in routine practice.

Figure 1: Eosinophilic bodies appearing as amorphous extracellular eosinophilic aggregates in FNAC smear of tuberculous lymphadenitis (Leishman stain, ×400)



Materials and Methods

A hospital-based prospective observational study was conducted in the Department of Pathology at a tertiary care center over a one-year period from February 2024 to January 2025. The study was approved by the Institutional Ethics Committee, and informed consent was obtained from all participants. The study included 200 consecutive patients presenting to the RNTCP clinic with clinically suspected tuberculous lymphadenitis. Eligible participants were adults (>18 years) with lymphadenopathy suggestive of tuberculosis, including those with concomitant sputum smear-negative pulmonary tuberculosis where applicable. Patients receiving anti-tubercular therapy, those with known malignancy, and cases subsequently diagnosed as reactive lymphadenitis were excluded. Fine-needle aspiration cytology (FNAC) was performed under strict aseptic precautions, and the aspirated material was processed for both cytomorphological and microbiological evaluation. Smears were stained with Leishman stain for morphological

assessment and Ziehl–Neelsen staining for the detection of acid-fast bacilli. Slides were independently reviewed in a blinded manner by 2 senior pathologists, and inter observer agreement was assessed. Cytological evaluation was systematically undertaken to identify the presence of granulomas, necrosis, and eosinophilic bodies. In all cases, parallel samples were analyzed using cartridge-based nucleic acid amplification testing (CBNAAT), which served as the reference standard for confirming Mycobacterium tuberculosis infection.

Statistical Analysis

Statistical analysis was performed using SPSS version 25.0. Sensitivity, specificity, PPV, and NPV were calculated. Chi-square test was used to assess association, and kappa statistics were used to evaluate agreement. Fisher's exact test was also applied where expected cell counts were less than 5. Ninety-five percent confidence intervals were calculated using the Wilson score method. A paired comparison between eosinophilic bodies and AFB staining among CBNAAT-positive cases was performed using McNemar's test. An exact test was applied due to zero values in one discordant cell. A p-value <0.05 was considered statistically significant

Results

Table 1: Demographic Characteristics (n = 200)

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	98	49%
	Female	102	51%
Age Group (years)	18–31	48	24%
	32–47	92	46%
	≥48	60	30%
Constitutional Symptoms	Present	80	40%
	Absent	120	60%

Table 2: Site Distribution of Lymphadenopathy

Site	Number of Cases (n)	Percentage (%)
Cervical	154	77%
Submandibular	20	10%
Submental	20	10%
Axillary	4	2%
Inguinal	2	1%
Total	**200**	**100%**

Table 3: Cytomorphological Findings

Cytological Feature	Number of Cases (n)	Percentage (%)
Necrotic aspirates	140	70%
Hemorrhagic aspirates	60	30%
Well-formed granulomas	15	7.5%
Eosinophilic bodies (EB)	175	87.5%

Table 4: AFB Smear vs CBNAAT

AFB Smear Result	CBNAAT Positive	CBNAAT Negative	Total
Positive	150	0	150
Negative	40	10	50
Total	**190**	**10**	**200**

Table 5: Eosinophilic Bodies vs CBNAAT

EB on Smear	CBNAAT Positive	CBNAAT Negative	Total
Positive	175	0	175
Negative	15	10	25
Total	**190**	**10**	**200**

Table 6: Comparative Diagnostic Performance of AFB Smear and Eosinophilic Bodies Using CBNAAT as Reference Standard (with 95% Confidence Intervals)

Parameter	AFB Smear (%)	95% CI (AFB)	Eosinophilic Bodies (%)	95% CI (EB)
Sensitivity	78.9 (150/190)	**72.5 – 84.2**	92.1 (175/190)	**87.3 – 95.2**
Specificity	100 (10/10)	**69.2 – 100**	100 (10/10)	**69.2 – 100**

Parameter	AFB Smear (%)	95% CI (AFB)	Eosinophilic Bodies (%)	95% CI (EB)
PPV	100 (150/150)	**97.5 – 100**	100 (175/175)	**97.9 – 100**
NPV	20 (10/50)	**11.2 – 33.0**	40 (10/25)	**23.4 – 59.3**

Table 7: Chi-Square Test for Association with CBNAAT

Test Variable	Chi-Square (χ^2)	Degrees of Freedom (df)	p-value	Interpretation
AFB vs CBNAAT	33.68	1	<0.001	Significant association
EB vs CBNAAT	95.00	1	<0.001	Highly significant association

Table 8: Kappa Agreement Analysis

Comparison	Kappa (κ)	Strength of Agreement
EB vs CBNAAT	0.44	Moderate agreement

Table 9 : Key Statistical Summary

Parameter	Observation
Total CBNAAT Positive Cases	190
Total CBNAAT Negative Cases	10
False Negatives (AFB)	40
False Negatives (EB)	15
Improvement in Sensitivity	+13.2%
Improvement in NPV	+20%

A total of 200 patients with clinically suspected tuberculous lymphadenitis were included in the study.

Among the study population, 102 patients (51%) were females and 98 (49%) were males, showing a slight female predominance. The majority of patients belonged to the 32–47 years age group (92 cases, 46%), followed by ≥48 years (60 cases, 30%) and 18–31 years (48 cases, 24%).

Constitutional symptoms such as fever, weight loss, and night sweats were present in 80 patients (40%), whereas 120 patients (60%) were asymptomatic (Table 1).

Cervical lymph nodes were the most commonly involved site, accounting for 154 cases (77%). Submandibular and submental lymph nodes were involved in 20 cases each (10%), while axillary (4 cases, 2%) and inguinal (2 cases, 1%) lymphadenopathy were less frequent (Table 2).

On cytological examination, necrotic aspirates were observed in 140 cases (70%), while 60 cases (30%) showed hemorrhagic aspirates. Well-formed granulomas were present in only 15 cases (7.5%).

Eosinophilic bodies (EBs) were identified in 175 cases (87.5%), indicating their frequent occurrence in cytological smears of tuberculous lymphadenitis (Table 3).

CBNAAT was used as the reference standard and was positive in 190 cases (95%) . Among the 200 cases studied, CBNAAT confirmed tuberculosis in 190 cases. On comparison, AFB smear demonstrated 150 true positive cases, while 40 cases were false negatives. Additionally, 10 cases were true negatives, and no false-positive cases were observed. In contrast, eosinophilic bodies (EBs) showed 175 true positive cases, with only 15 false negatives. Similar to AFB, 10 cases were true negatives, and no false-positive cases were identified (Tables 4 and 5).

The diagnostic performance of both methods revealed that eosinophilic bodies had a higher sensitivity (92.1%) compared to AFB staining (78.9%). Both methods demonstrated 100% specificity and positive predictive value (PPV). However, the negative predictive value (NPV) of eosinophilic bodies (40%) was higher than that of AFB staining (20%). Overall, eosinophilic bodies showed superior sensitivity and improved NPV, indicating better detection of true positive cases, particularly in smear-negative scenarios (Tables 6).

Chi-square analysis demonstrated a statistically significant association between both diagnostic methods and CBNAAT (AFB vs CBNAAT: $\chi^2 = 33.68$, $p < 0.001$; EB vs CBNAAT: $\chi^2 = 95.00$, $p < 0.001$). Fisher's exact test, applied due to small expected cell counts, also showed statistically significant associations ($p < 0.001$). The higher

chi-square value observed for eosinophilic bodies indicates a stronger association with CBNAAT positivity (Table 7).

On paired comparison among CBNAAT-positive cases, eosinophilic bodies detected 25 additional cases that were negative on AFB staining, while no cases were AFB positive and EB negative. McNemar's test demonstrated that this difference was statistically significant ($p < 0.001$). The kappa coefficient between eosinophilic bodies and CBNAAT was 0.44, indicating moderate agreement (Table 8). Interobserver agreement for identification of eosinophilic bodies on cytological smears was assessed and demonstrated moderate agreement, with a kappa coefficient (κ) of 0.46

Discussion

Tuberculous lymphadenitis remains the most common form of extrapulmonary tuberculosis and continues to pose significant diagnostic challenges due to its paucibacillary nature and heterogeneous cytomorphological presentation [2,3]. In such settings, reliance on conventional diagnostic methods often results in underdiagnosis, particularly in smear-negative cases. The present study was undertaken to evaluate the role of eosinophilic bodies (EBs) as an adjunct cytological marker in comparison with AFB staining, using CBNAAT as the reference standard.

In the present study, a slight female predominance (51%) and peak incidence in the 32–47-year age group (46%) were observed, which is consistent with previously reported epidemiological patterns of extrapulmonary tuberculosis [2,9]. The observation that 60% of patients were asymptomatic highlights the diagnostic limitation of clinical assessment alone and emphasizes the importance of cytological and laboratory-based confirmation. Similar findings have been reported in previous studies, where a substantial proportion of patients with tuberculous lymphadenitis lacked constitutional symptoms, leading to delayed diagnosis [9,10].

Cervical lymph nodes were the most commonly involved site (77%), followed by submandibular and submental lymph nodes. This pattern is well documented in the literature, where cervical lymphadenopathy accounts for the majority of cases of tuberculous lymphadenitis [10,11]. The predilection for cervical nodes is attributed to lymphatic drainage patterns and the frequent involvement of upper aerodigestive tract-associated lymphoid tissue.

Cytomorphological evaluation in this study demonstrated that necrosis was the predominant finding (70%), while well-formed granulomas were observed in only 7.5% of cases. This finding supports previous reports indicating that classical granulomatous features may be absent in a significant proportion of cases, particularly in early disease, immunocompromised individuals, or in cases with high necrotic load [3,4,12]. The absence of granulomas can significantly reduce the diagnostic yield of FNAC when relying solely on traditional criteria.

A notable finding of this study is the high prevalence of eosinophilic bodies (87.5%) in cytological smears. These structures were frequently identified even in cases lacking classical granulomatous features, suggesting their potential role as a supplementary morphological marker. Although their exact origin remains unclear, eosinophilic bodies are believed to represent degenerative cellular debris associated with caseous necrosis, as described in earlier cytological studies [8,12]. Their consistent presence in a majority of cases in the present study highlights their diagnostic relevance.

Eosinophilic bodies observed in cytological smears likely represent aggregated products of cellular degeneration within areas of caseous necrosis. These structures arise from the breakdown of inflammatory cells, leading to accumulation of denatured proteins, nucleoprotein debris, and lipid-rich material, which exhibit eosinophilic staining characteristics. Their frequent occurrence in necrotic aspirates suggests that they are a morphological manifestation of advanced tissue destruction in tuberculous lymphadenitis [8,12,17].

In contrast to acid-fast bacilli detection, which depends on the presence of intact mycobacteria, eosinophilic bodies reflect the host tissue response and therefore remain identifiable even in cases where bacilli are sparse or structurally degraded. This explains their higher sensitivity in necrotic and paucibacillary lesions, where Ziehl–Neelsen staining often yields false-negative results due to loss of bacillary integrity [5,13,18].

From a practical perspective, the identification of eosinophilic bodies can be easily incorporated into routine FNAC evaluation without additional cost or infrastructure. Their presence, particularly

in necrotic smears with negative AFB staining, may serve as a useful indicator to prompt further molecular testing or support early clinical suspicion of tuberculosis, especially in resource-constrained settings [6,7,15]. However, given their non-specific nature, eosinophilic bodies should be interpreted in conjunction with other cytomorphological features and clinical findings [3,4,17].

When compared with CBNAAT, eosinophilic bodies demonstrated higher sensitivity (92.1%) than AFB staining (78.9%), while both methods showed 100% specificity and PPV. This improvement in sensitivity resulted in a marked reduction in false-negative cases (15 vs 40), indicating that EBs are particularly useful in detecting cases that may be missed by AFB staining. These findings are in agreement with previous studies that have demonstrated the limited sensitivity of AFB staining in paucibacillary conditions and emphasized the need for adjunct diagnostic markers [5,13].

The negative predictive value (NPV) of eosinophilic bodies (40%) was higher than that of AFB (20%), suggesting improved ability to exclude disease, although still limited. The relatively low NPV observed in this study is likely attributable to the high prevalence of tuberculosis in the study population. Similar trends have been reported in other high-burden settings, where diagnostic tests tend to show high PPV but relatively low NPV [13].The significantly higher sensitivity of eosinophilic bodies compared to AFB staining was further confirmed by paired analysis using McNemar's test, which demonstrated a statistically significant difference ($p < 0.001$). This supports the superiority of eosinophilic bodies as an adjunct marker, particularly in smear-negative cases

Statistical analysis further reinforced these findings. The significantly higher chi-square value for EBs ($\chi^2 = 95.00$) compared to AFB ($\chi^2 = 33.68$) indicates a stronger association with CBNAAT-confirmed disease. The kappa value of 0.44 indicates moderate agreement between EB and CBNAAT. Although this level of agreement is not strong, it is clinically meaningful when interpreted in conjunction with the high sensitivity and absence of false-positive cases. Similar levels of agreement have been reported in studies evaluating adjunct cytological markers in tuberculosis [14].

Molecular diagnostic tools such as Xpert MTB/RIF have significantly improved the rapid detection of tuberculosis, particularly in extrapulmonary samples [6,7]. However, their widespread use is often limited by cost, infrastructure requirements, and accessibility, especially in peripheral healthcare settings [7,15]. In such contexts, reliance on cytological evaluation remains essential, and the identification of additional morphological markers such as eosinophilic bodies can significantly enhance diagnostic accuracy.

From a practical standpoint, eosinophilic bodies represent a simple, cost-effective, and reproducible cytological feature that can be easily incorporated into routine FNAC evaluation without the need for additional resources. Their use as an adjunct marker may facilitate earlier diagnosis and timely initiation of treatment, thereby reducing disease burden and transmission in high-prevalence settings.

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