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DIAGNOSTIC ACCURACY OF FNAC AND MANTOUX TEST IN TUBERCULOUS LYMPHADENITIS: A TWO-PRONGED APPROACH TO DIAGNOSIS

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ABSTRACT:
Introduction: Tuberculous lymphadenitis (LNTB) is the most common form of extrapulmonary tuberculosis (EPTB), often posing diagnostic challenges due to its varied clinical presentations. Fine Needle Aspiration Cytology (FNAC) and the Mantoux test are widely utilized for its diagnosis. This study evaluates the diagnostic accuracy of FNAC and the Mantoux test in detecting tubercular lymphadenitis.
Methods: A total of 150 patients with clinically suspected tuberculous lymphadenopathy were included. The study was conducted at the Department of Pathology, Saveetha Medical College, Chennai, from January 2023 to December 2023. Informed consent was obtained from all participants. FNAC was performed using a 20-23 gauge needle, and smears were stained with Hematoxylin and Eosin (H&E) and Papanicolaou (PAP) stains. The Mantoux test was conducted using an intradermal injection of 0.1 mL of purified protein derivative (PPD). Cases were classified into four cytomorphological patterns based on FNAC findings.
Results: Of the 150 cases, 92 (61.3%) were male, and 58 (38.7%) were female, with a mean age of 41.57 years. The most affected lymph nodes were cervical (89.3%). Mantoux positivity was observed in 135 (90%) cases. FNAC revealed four cytomorphological patterns: caseating epithelioid granulomas (44%), epithelioid cell granulomas without necrosis, necrosis without granulomas, and necrosis with suppuration. The Mantoux test exhibited a high sensitivity (100%) and a positive predictive value (90%).
Conclusion: The combined use of FNAC and the Mantoux test enhances the diagnostic accuracy of tuberculous lymphadenitis. FNAC provides a rapid and cost-effective method, while the Mantoux test serves as a useful adjunct, particularly in endemic regions. A positive Mantoux result in patients with unexplained lymphadenopathy should prompt further FNAC or biopsy to confirm the diagnosis. Integrating these diagnostic tools enables early detection and effective management of tubercular lymphadenitis.

INTRODUCTION

Tuberculosis (TB) is one of the oldest known infectious diseases, with the *Mycobacterium* genus tracing its origins back over 150 million years (10). Archaeological findings, such as skeletal abnormalities in Egyptian mummies, provide historical evidence of TB, and depictions of Pott's disease in ancient art further suggest its longstanding presence in human history (11). Despite advancements in medical science, TB remains a major global health burden. According to the World Health Organization (WHO), it is the leading cause of death from a single infectious agent and ranks among the top ten causes of mortality worldwide. The 2020 WHO Global TB Report estimated that around 10 million individuals contracted TB, resulting in approximately 1.4 million fatalities (12).
TB continues to pose a severe public health challenge, particularly in developing countries, where it remains one of the primary causes of illness and death (1). It is a chronic granulomatous infection primarily caused by

Mycobacterium tuberculosis and, in rare instances, by *Mycobacterium bovis* through the consumption of unpasteurized dairy products or by atypical mycobacterial infections (5). Each year, TB accounts for an estimated 8 million new infections and 3 million related deaths. The prevalence of TB is rising in resource-limited regions, often linked to poor sanitation and an increasing number of immunocompromised individuals, particularly those with acquired immunodeficiency syndrome (AIDS) (7).

Although TB primarily affects the lungs, it can also manifest in extrapulmonary sites, including the head and neck region. Pulmonary tuberculosis (PTB) is the most common presentation, while extrapulmonary tuberculosis (EPTB) is relatively rare, affecting only 0.05% to 5% of TB patients (3). Due to its low prevalence, TB is not always immediately considered in the differential diagnosis of head and neck lesions (8). WHO classifies TB into PTB and EPTB based on the site of infection, with EPTB often presenting as peripheral lymphadenopathy. It can also affect other organs, including the skin, brain, soft tissues, intestines, appendix, and genitourinary tract (12). In 2019, EPTB constituted 16% of the 7.1 million newly diagnosed TB cases worldwide. India reports lymph node TB (LNTB), or tuberculous lymphadenitis, as the most frequent form of EPTB, accounting for about 35% of all EPTB cases. That same year, the estimated TB incidence in India was 2.1 million, with 385,254 cases classified as EPTB (12).

Despite the availability of several diagnostic tools, diagnosing tuberculous lymphadenitis remains challenging. Fine-needle aspiration cytology (FNAC) is a widely used, minimally invasive outpatient diagnostic method that is well-tolerated by patients (6). It is considered an effective technique for identifying TB through cytomorphological examination, particularly when epithelioid cells are present with or without caseation necrosis. However, since epithelioid cells may also be found in other conditions (4), additional diagnostic tests are often required. The Mantoux test plays a crucial role in diagnosing TB, particularly in cases where FNAC findings are inconclusive. This study aims to assess the diagnostic value of FNAC in tuberculous lymphadenopathy and evaluate the significance of the Mantoux test in suspected cases.

MATERIAL AND METHOD

This study was carried out in the Department of Pathology at Saveetha Medical College, Thandalam, Chennai, over a one-year period from January 2023 to December 2023. Participants of all age groups and both genders were included, with informed consent obtained from each patient before enrollment. Detailed demographic and clinical data, such as age, gender, medical history, the specific lymph node groups involved, and the type of aspirate collected during fine-needle aspiration cytology (FNAC), were systematically documented.

Ethical clearance for the study was duly obtained from the institutional ethics committee. The collection of aspiration samples, clinical data compilation, and subsequent analysis were performed exclusively by authorized personnel, adhering strictly to the approved research protocol.

Sample Collection and Processing:

A total of 150 patients were included in this study, comprising individuals with nonspecific lymphadenopathy characterized by lymph nodes larger than 1 cm without an identifiable cause. These patients underwent the Mantoux test. FNAC was performed on individuals presenting with superficial palpable cervical lymph nodes, with or without associated pain. Prior to the procedure, informed consent was obtained from all participants.

Preparation and Study Sample: The Mantoux test was administered through an intradermal injection of 0.1 mL of purified protein derivative (PPD) on the flexor surface of the forearm. After 72 hours, the test was considered positive if an erythematous induration of 10 mm or more was observed. In patients who tested positive, FNAC was subsequently performed to assess for tuberculosis. The procedure involved the use of a 20-23 gauge needle attached to a disposable 10 mL plastic syringe. The aspirated material was smeared onto 2-3 slides, fixed in 95% ethyl alcohol, and stained using Hematoxylin and Eosin (H&E) and Papanicolaou (PAP) staining techniques. All stained smears were examined, and diagnoses were made based on cytomorphological characteristics.

CYTOLOGICAL DIAGNOSIS:

The cases were categorized into four cytomorphological patterns, following the classification system adapted from Das et al. (1990):

- **Pattern A**: Caseous necrosis with epithelioid cell granulomas.
- **Pattern B**: Presence of epithelioid cell granulomas without caseous necrosis.
- **Pattern C**: Caseous necrosis without epithelioid granulomas.
- **Pattern D**: Acute suppuration.

FNAC smears were considered cytomorphologically indicative of tuberculosis if they exhibited caseous necrosis with or without epithelioid granulomas, specifically corresponding to Patterns A and C (9).

Inclusion Criteria:

Patients clinically suspected of having tuberculous lymphadenitis were included in the study.

Exclusion Criteria:

1. Patients who had received anti-tuberculosis treatment within 60 days before sample collection.
2. Lymphadenopathy cases suspected to be of malignant origin.
3. Inadequate aspirated sample material.
4. Lack of informed consent from the participant.

RESULTS:

Among the 150 diagnosed cases of tuberculosis, patient ages ranged from 20 to 70 years. Of these, 92 cases (61.33%) were male, while 58 cases (38.66%) were female, as presented in Table 1. In this study, the cervical lymph node group was the most commonly affected. The highest number of cases occurred in individuals in their second and third decades of life. The male-to-female ratio was approximately 1.59:1, with a mean age of around 41.57 years.

Aspiration samples from lymph nodes diagnosed with tuberculous lymphadenopathy exhibited varying cytomorphological features. Some cases presented with epithelioid cell granulomas, occasionally accompanied by Langerhans giant cells, and necrosis interspersed within lymphoid cells. In other instances, the aspirates contained epithelioid cell granulomas without necrosis or caseation, while some samples consisted solely of necrotic material, characterized by diffuse granular debris.

Table 1 - Age Distribution according to Gender

Age group (years)	Male No. (%)	Female No. (%)	Total No. (%)
21 - 30	29 (31.5)	12 (20.6)	41 (27.3)
31 - 40	23 (25)	16 (27.5)	39 (26)
41 - 50	15 (16.3)	13 (22.4)	28 (18.7)
51 - 60	13 (14.1)	9 (15.5)	22 (14.6)
61 - 70	12 (13)	8 (13.7)	20 (13.3)
Total	92 (61.33)	58 (38.66)	150

Table2: Profile of demographic and clinical features:

Anatomical site	
Cervical	134 (89.3%)
Axillary	14 (9.33%)
Inguinal	2 (1.33%)
Size (cm)	
≤ 2	43 (28.6%)
2.1 to 4	84 (56%)
4.1 to 6	18 (12%)
> 6	5 (3.33%)
Aspirate appearance	
Purulent	38(25.3%)
Hemorrhagic	97 (64.6%)
Caseous	15 (10%)

Among the 150 tuberculosis cases examined, 135 cases (90%) tested positive for the Mantoux test (Fig. 1), while the remaining 15 cases (10%) tested negative.
Based on cytomorphological characteristics, the cases were classified into four distinct patterns:

1. **Pattern A – Caseating Epithelioid Granuloma**: Characterized by the presence of epithelioid granulomas along with caseous necrosis (Fig. 2).
2. **Pattern B – Epithelioid Cell Granuloma Without Necrosis**: Smears exhibiting only epithelioid cell granulomas without any signs of necrosis (Fig. 3).
3. **Pattern C – Caseating Tuberculous Lymphadenitis**: Identified by smears containing only caseous necrotic material without granulomas (Fig. 4).
4. **Pattern D – Caseating Epithelioid Granuloma with Superadded Suppuration**: Smears demonstrating a combination of epithelioid granulomas, caseous necrotic material, and additional suppurative inflammation (Fig. 5).

Fig.1- Montoux test shows Positivity

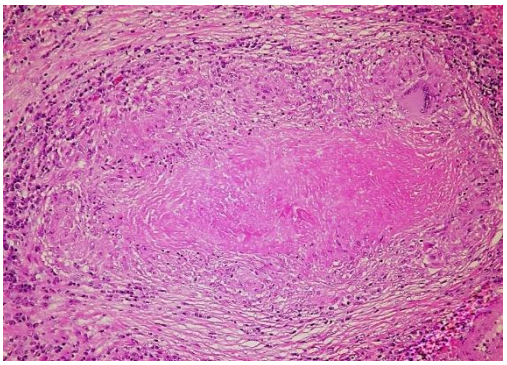


Fig.2- Granuloma with necrosis, H&E stain (40x)

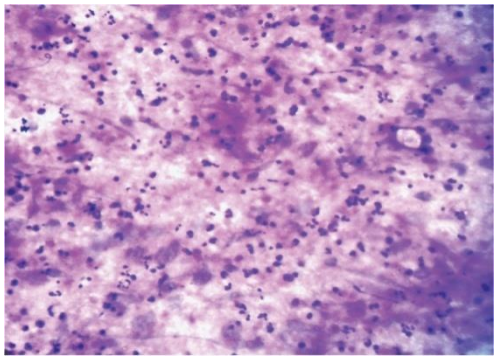


Fig.3- Granuloma alone, H&E stain (40x)

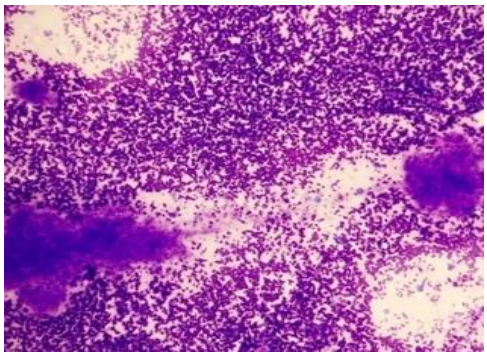


Fig.4- Smears shows only Necrosis, H&E stain (40x)

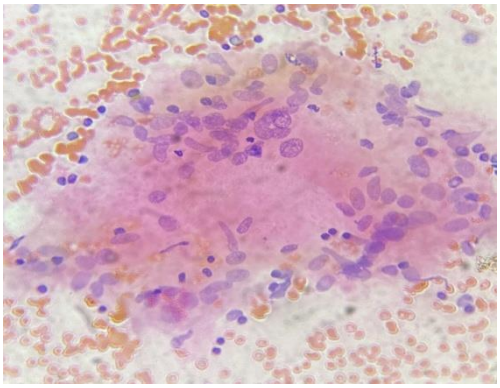
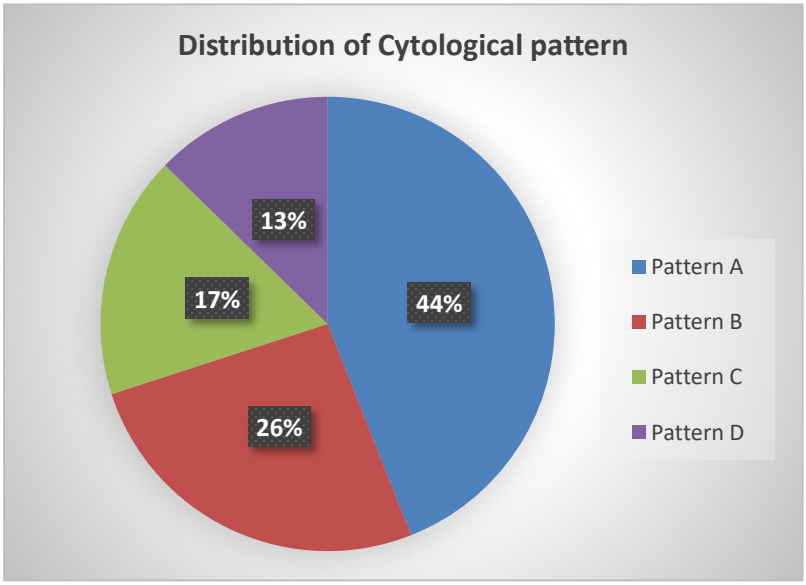


Fig.5- Granuloma with superadded suppuration, H&E stain (40x)

Table 3: Number of cases distribution according to the Cytomorphological pattern:

CYTOLOGICAL PATTERN	NUMBER OF CASES	PERCENTAGE
Granuloma and necrosis	66	44
Granuloma alone	39	26
Necrosis alone	26	17.3
Granuloma with superadded infection	19	12.7



DISCUSSION

Tuberculous lymphadenitis (LNTB) is the most common form of extrapulmonary tuberculosis (EPTB), as highlighted by Tadesse et al. (13). Although early diagnosis and appropriate treatment can effectively manage the condition, diagnosing LNTB remains challenging due to its ability to mimic other diseases.

In this study, the age of affected individuals ranged from 20 to 70 years. The highest incidence (41%) was observed in the second and third decades of life, followed by a gradual decline, which is consistent with findings from Ahmad et al. and Hemalatha et al. (14,15). A male predominance was noted, with a male-to-female ratio of 1.59:1, aligning with observations made by Ahmad et al. (14). Mycobacterium tuberculosis primarily reaches the cervical lymph nodes via the tonsillar lymphoid tissue, explaining why cervical lymph nodes were the most commonly affected (89.3%), while inguinal lymph nodes were the least involved (1.33%). This distribution aligns with findings from studies conducted by Nidhi et al. and Chand et al. (16,17).

Diagnosing LNTB through microbiological methods is often challenging due to inconsistent laboratory results. Several diagnostic tools, including the Mantoux test, fine needle aspiration cytology (FNAC), acid-fast bacilli (AFB) smear microscopy, culture, and GeneXpert MTB/RIF, are utilized for detection. Each method has its strengths and limitations. Although culture remains the gold standard, it is time-consuming and may yield false-negative results in patients already undergoing tuberculosis treatment since it only detects viable bacteria. AFB smear microscopy can also be unreliable due to the low bacterial load in samples. FNAC, on the other hand, is a quick and cost-effective diagnostic approach, with the presence of epithelioid granulomas and caseous necrosis being highly indicative of tuberculosis, especially in endemic regions like India. GeneXpert MTB/RIF offers the advantage of detecting Mycobacterium tuberculosis and rifampicin resistance within a few hours (12).

Regarding aspirate characteristics in this study, the most common type was hemorrhagic (64.6%), followed by purulent (25.3%), with caseous aspirate being the least frequent (10%). These findings are in agreement with studies conducted by Hemalatha et al. and Masilamani et al. (15,18).

The most frequently observed cytomorphological pattern was the presence of epithelioid granulomas with caseous necrosis, which accounted for 44% of cases. Similarly, Gosavi et al. (19) identified this pattern in 60% of cases, while Gupta et al. (20) documented it in 52.5%. In contrast, Paliwal et al. (16) reported necrosis without epithelioid granulomas as the most common presentation (39.2%). Chand et al. (17) observed that caseous necrotic material with epithelioid granulomas and giant cells was the dominant cytological pattern. Blood-tinged aspirates were most frequently associated with Patterns A and B, whereas purulent and caseous aspirates were more prevalent in Patterns C and D. These observations are consistent with reports by Hemalatha et al. (15) and Masilamani et al. (18).

The Mantoux test (MT) is widely used as an auxiliary diagnostic tool for tuberculosis. However, its diagnostic accuracy is limited due to its low sensitivity and specificity. In this study, the sensitivity of the Mantoux test was 100%, with a positive predictive value (PPV) of 90% and a negative predictive value (NPV) of 100%. Garde et al. (21) underscored the importance of the Mantoux test in diagnosing tuberculosis in pediatric patients, with 10 out of 15 cases showing positive results. In our study, 90% of patients with tubercular lymphadenopathy exhibited Mantoux positivity, often with strong reactions exceeding 20 mm. False-positive Mantoux test results may arise due to infection with non-tuberculous mycobacteria or prior Bacillus Calmette-Guérin (BCG) vaccination (22). Therefore, integrating the Mantoux test with FNAC improves diagnostic accuracy.

CONCLUSION

This study highlights the importance of a combined diagnostic approach using FNAC and the Mantoux test for detecting tubercular lymphadenitis. While FNAC provides rapid, cost-effective, and cytomorphological confirmation, the Mantoux test serves as a valuable supplementary tool, particularly in endemic regions. Despite its limitations, the Mantoux test remains relevant in clinical settings, especially when diagnostic uncertainty persists. Given its high sensitivity, a positive Mantoux test should prompt further evaluation through FNAC or biopsy to ensure an accurate diagnosis. Integrating these diagnostic modalities enhances the detection of tubercular lymphadenitis, facilitating early intervention and improving patient outcomes.

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CONFLICT OF INTEREST: - The authors have no conflict of interest and nothing to declare.

AUTHOR CONTRIBUTIONS: -

R. Sowmya and *H. Volga* contributed to the conceptualization, visualization, and overall project administration of the study. *R. Sowmya* played a key role in drafting the original manuscript and managing data curation, while *H. Volga* was responsible for validation and formal analysis. All authors actively participated in revising the manuscript and have approved the final submitted version.

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