

COMPARISON OF OUTCOME OF DIFFERENT DIAGNOSTIC MODALITIES IN TUBERCULAR CERVICAL LYMPHADENITIS

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ABSTRACT

BACKGROUND

There are nearly 9 million new cases and 2 million deaths from tuberculosis worldwide every year.¹ The incidence of mycobacterial lymphadenitis has increased in parallel with the increase in the incidence of mycobacterial infection worldwide. Tubercular lymphadenitis is seen in nearly 35 percent of extrapulmonary tuberculosis. Cervical lymph nodes is the most common site of involvement.

MATERIALS AND METHODS

Every patient out of 116 patients with TB cervical lymphadenitis was investigated with chest x-ray, sputum for AFB, Mantoux test, USG neck, FNAC, FNAC culture on LJ media and excision biopsy.

RESULTS

Biopsy of cervical lymph node is the best investigation for diagnosis of tubercular lymphadenitis and hence considered as a gold standard. The sensitivity of Mantoux test was 82.4% and specificity was 68.6%. Sensitivity of FNA culture on LJ media was 84.6% and specificity was 72.3%. Sensitivity of FNAC was 84.1% and specificity was 65.5%. Sensitivity of ultrasonography was 92.4%, whereas specificity was 64.2% and sensitivity of excision biopsy was 96.4% and specificity was 88.4%.

CONCLUSION

On comparison with lymph node biopsy, ultrasonography of neck showed high sensitivity followed by FNA culture on LJ medium, FNAC and Mantoux test, whereas on comparing specificity, FNA culture on LJ medium had a high specificity followed Mantoux test, FNAC and ultrasonography. To achieve a high specificity and sensitivity for diagnosis of tubercular lymphadenitis, a combination of two or more investigations can be used, but more studies are required to evaluate the optimal combination of these investigations for accurate and cost-effective analysis.

KEYWORDS

Tuberculosis (TB), Tubercular Cervical Lymphadenitis, Mantoux Test, FNAC, FNA Culture on LJ Medium, USG Neck, Excision Biopsy.

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BACKGROUND

Mycobacterial lymphadenitis has plagued humanity since long. There are nearly 9 million new cases and 2 million deaths from tuberculosis worldwide every year. The incidence of mycobacterial lymphadenitis has increased in parallel with the increase in the incidence of mycobacterial infection worldwide. Tuberculosis lymphadenitis is seen in nearly 35 percent of extrapulmonary tuberculosis cases,

which constituted about 15 to 20 percent of all cases of tuberculosis. In HIV positive patients, extrapulmonary tuberculosis accounts for up to 53 to 62 percent cases of TB.^{2,3,4} Cervical lymph nodes is the most common site of involvement and reported in 60% to 90% patients with or without involvement of other lymphoid tissue.^{5,6} Cervical lymphadenitis, which is also referred to as scrofula, maybe one of the manifestation of a systemic tuberculosis disease or a unique clinical entity localised to neck. Mycobacterium tuberculosis is the most common causative agent in India.^{7,8} The incidence of mycobacterial lymphadenitis primarily depends on the endemicity of the Mycobacterium tuberculosis. Lymphadenopathy due to Nontuberculous Mycobacterium (NTM) is uncommonly reported from India.² In nontuberculous lymphadenitis, Mycobacterium avium - intracellular complex is the most common causative agent. Apart from a focused history and detailed clinical examination, several other studies are required for

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conforming the diagnosis of lymph node tuberculosis. To name a few of them are Mantoux test, chest radiography, Computerised Tomography (CT) of neck and chest, USG neck, FNAC, visualisation of mycobacteria on smear stain for AFB or mycobacterial culture and excision biopsy of lymph node, which remains the gold standard for diagnosis of lymph node tuberculosis.

Though the excision biopsy is considered as gold standard investigation for the diagnosis of lymph node tuberculosis, it is not freely available in rural areas and suburbs of our country. Also, being a little expensive, invasive surgical modality of investigation and for cosmetic reasons many patients of tubercular lymphadenitis are not willing to undergo this investigation modality. Hence, we conducted a study to assess the outcome of other easily available, noninvasive and comparatively cheaper diagnostic modalities used for diagnosis of tubercular cervical lymphadenitis and compared their yield with biopsy, which is considered as gold standard investigation.

Aims and Objectives

1. To study outcome of different diagnostic modalities in tubercular cervical lymphadenopathy.
2. To compare the yield of these diagnostic modalities with that of excision biopsy, which is considered as a gold standard.

MATERIALS AND METHODS

This is a prospective analytical diagnostic study conducted from August 2014 to October 2016 at MGM Medical College and Hospital, Aurangabad.

Total 116 patients having clinical diagnosis of tubercular cervical lymphadenopathy were included in this study. Variables included for this study were age, sex, presenting symptoms, history of contact with tuberculosis patients and previous history of pulmonary or extrapulmonary tuberculosis.

Inclusion Criteria

All clinically-diagnosed patients with tubercular cervical lymphadenopathy who were willing to undergo investigations.

Exclusion Criteria

1. Patients below 18 years of age.
2. Cervical lymphadenopathy of nontubercular aetiology.

Following procedures and investigations were performed in each patients.

Physical examination, chest x-ray, sputum for AFB, HIV, Mantoux test, USG neck (high frequency), FNAC, FNA culture on LJ medium and excision biopsy.

RESULTS

Chest X-Ray

All patients enrolled were subjected for chest x-ray frontal view to look for parenchymal opacities or mediastinal lymphadenopathy. Out of 116 patients, 26 patients (22.4%) showed chest x-ray changes in the form of parenchymal

opacities and mediastinal lymphadenopathy. 90 patients (77.6%) out of total 116 patients showed normal chest x-ray.

Chest X-Ray Changes	Number of Patients	Percentage
X-ray showing opacities and mediastinal lymphadenopathy	26	22.4%
Normal chest x-ray	90	77.6%
Chest X-Ray Findings		

Sputum for AFB

Sputum of all the patients enrolled in this study was subjected to staining for acid-fast bacilli irrespective of chest x-ray changes and presence of respiratory symptoms. Out of them, 13 patients (11.2%) were sputum positive and 103 patients (88.8%) were negative for acid-fast bacilli.

Sputum for AFB	Number of Patients	Percentage
Positive	13	11.2%
Negative	103	88.8%
Sputum for AFB		

Mantoux Test

All patients enrolled in the study were subjected to Mantoux test out of which 66 patients (56.9%) showed induration more than 10 mm suggestive of positive test and 50 patients (43.1%) showed no induration or less than 10 mm suggestive of negative Mantoux test. Sensitivity is 82.4% and specificity is 68.6% (P value 0.035).

Mantoux	Number of Patients	Percentage
Positive	66	56.9%
Negative	50	43.1%
Mantoux Test Interpretation		

FNA Culture on LJ Medium

All patients with cervical lymphadenopathy were subjected to fine needle aspiration culture. Aspiration from the lymph nodes were sent for culture on Lowenstein-Jensen medium. 55 patients (47.4%) out of 116 patients showed growth on Lowenstein-Jensen medium and 61 patients (52.6%) did not show any growth. Sensitivity is 84.6%, specificity is 72.3% (P value is 0.023).

FNAC Culture on LJ Medium	Number of Patients	Percentage
Positive	55	47.4%
Negative	61	52.6%
Fine Needle Aspiration Culture on LJ Medium		

Fine Needle Aspiration Cytology (FNAC)

All patients enrolled in the study were subjected to FNAC (fine needle aspiration cytology) of the lymph nodes. In 82 patients (70.7%), cytology was reported as tubercular lymphadenitis, whereas in 34 patients (29.3%), it was reported as nonspecific or chronic inflammatory

lymphadenitis. Sensitivity is 84.1% and specificity is 65.5% (P value 0.048).

FNAC	Number of Patients	Percentage
FNAC showing tubercular lymphadenitis	82	70.7%
Need biopsy for confirmation	34	29.3%
Fine Needle Aspiration Cytology (FNAC)		

Ultrasonography

All patients enrolled were subjected to ultrasonography of neck. Out of 116 patients, in 85 patients (73.3%) ultrasonography of neck was reported as suggestive of tubercular cervical lymphadenopathy where in other 31 patients (26.7%), it was reported as nonspecific or chronic inflammatory lymphadenitis. Sensitivity is 92.4%, specificity is 64.2% (P value is 0.019).

USG Neck	Number of Patients	Percentage
S/o tuberculosis	85	73.3%
Chronic inflammatory /nonspecific lymphadenitis	31	26.7%
Ultrasonography of Neck		

Excision Biopsy

All patients were subjected for excision biopsy. Out of 116 patients, 99 patients (85.3%) were reported as tubercular lymphadenitis and 17 patients (14.7%) were reported as nonspecific or chronic inflammatory lymphadenitis. Sensitivity is 96.4%, specificity is 88.4% (P value is 0.041).

Biopsy	Patients	Percentage
S/o tuberculosis	99	85.3%
Chronic inflammatory/nonspecific lymphadenitis	17	14.7%
Excision Biopsy		

Comparison of Mantoux Test with Excision Biopsy

The sensitivity of Mantoux test as compared with biopsy was found to be 82.4%, whereas specificity was 68.6% with a significant 'p' value of 0.035.

Comparison of FNA Culture on LJ Medium with Excision Biopsy

The sensitivity of FNA culture as compared to biopsy was 84.6% and specificity was 72.3% with p value of 0.023.

Comparison of FNAC with Excision Biopsy

The sensitivity of FNAC as compared to biopsy was 84.1% and specificity was 65.5% with p value of 0.048.

Comparison of Ultrasonography with Excision Biopsy

The sensitivity of ultrasonography as compared to biopsy was 92.4%, whereas specificity was 64.2% and p value of 0.019.

DISCUSSION

The current study was conducted to compare the diagnostic yields of Mantoux test, FNA culture on LJ medium, FNAC and USG neck in cases of cervical tubercular lymphadenitis keeping excision biopsy as a gold standard diagnostic modality. The objective of the study was to ascertain the overall diagnostic yields of Mantoux test, FNA culture on LJ medium, FNAC and USG neck for diagnosis of cervical tubercular lymphadenopathy. This was a prospective study conducted in the Department of Respiratory Medicine, MGM Medical College and Hospital, Aurangabad, after obtaining the Ethics Committee Approval.

Mantoux Test

Our study reported 66 patients with positive Mantoux test (56.9%) and 50 patients with negative Mantoux test (43.1%). Sensitivity is 82.4% and specificity is 68.6%. The study conducted by Zuber Ahmad et al. A total of 240 patients were studied out of which 156 patients (65%) were positive for Mantoux test and 84 patients were negative (35%) tuberculin test, t = 5.80, p <0.05.

Tuberculin skin testing is the cheapest and safe method for detection of present or past infection with mycobacterium tuberculosis organism. In our study, 56.9% patients were tuberculin test positive. The reported reactivity of tuberculin test in the literature ranged from none to very strong.⁹ Furcolow¹⁰ and Johnston¹¹ showed 99% positive test while Smith found 20-30% negative reactions.¹² A large number of factors have been reported⁹ to cause decreased ability to respond to tuberculin. Low sensitivity of tuberculin test in our study also might be due to such factors. Thus, tuberculin negativity did not rule out tuberculosis.

FNA Culture on LJ Medium

A study conducted by VC Kishore Reddy et al showed 45% that is 71 positive culture by LJ medium out of 157 aspirates. In our study, out of total 116 aspirates, 55 were (47.4%) culture positive, whereas 61 (52.6%) were culture negative. Sensitivity was 84.6% and specificity was 72.3%. Average duration taken for positive culture was 42 days (range 21-56 days). All the culture isolates were identified as Mycobacterium tuberculosis.

FNAC

In our study, FNAC was reported as tubercular lymphadenitis in 82 patients (70.7%) out of 116 and non-tubercular in 34 patients (29.3%). Sensitivity was 84.1% and specificity was 65.5%. Study conducted by Zuber Ahmad et al showed 168 positive (70%) and 72 showed negative (30%) out of 240 patients FNAC t=3.20, p >0.05 and study conducted by BC Jha, et al¹³ FNAC revealed a positive diagnosis in 85.7% of the patients.

Recently, there have been a number of reports on the value of Fine Needle Aspiration Cytology (FNAC) in the diagnosis of tuberculosis lymphadenitis with claims of sensitivity and specificity of 80-90% and diagnostic accuracy above 80%.¹⁴

The study by Jha BC et al¹³ reported a sensitivity of 92.8% in diagnosing tubercular lymphadenitis. Dandapat MC et al reported a sensitivity of 83% for tuberculosis.⁶

The study by Chao SS et al showed sensitivity of 88% and specificity of 96% for the same. Prasad RR et al¹⁵ studied 2216 cases and noted sensitivity and specificity of 84% and 95% respectively for tubercular lymphadenitis.

Ultrasonography

Ultrasonography findings have a high accuracy in differentiating benign from malignant cervical lymph nodes. According to a study conducted by Jun Ho Park et al,¹⁶ out of a study group of 79 patients, 40 patients (50.6%) were diagnosed as tubercular cervical lymphadenitis on ultrasonography and the diagnosis was confirmed by sonography-guided FNAC or PCR. In comparison to this, our study showed that out of 116 patients, 85 patients (73.3%) sonography of neck was reported as suggestive of tubercular lymphadenitis and 31 patients (26.7%) were reported as chronic inflammatory/nonspecific lymphadenitis. Sensitivity was 92.4% and specificity was 64.2%.

Histopathology

The literature has classically supported excision biopsy as the definitive diagnostic procedure for diagnosis of lymph node TB.¹⁷ Identification of caseating granulomatous inflammation with Langerhans giant cells supports a diagnosis of TB. Though histopathology is most rewarding for diagnosis of cervical lymphadenitis, its feasibility is limited due to lack of facilities in peripheral healthcare centres and its non-acceptability as it is an invasive procedure.

Study conducted by Abdurehman Eshete et al¹⁸ showed 85% positive results for excision biopsy. Another study conducted by P Bhargava et al¹⁹ showed 98.11% positive results for excision biopsy. In comparison with these two studies, our study showed positive result in 99 patients (85.3%) out of 116 and 17 patients (14.7%) were reported as negative. Study conducted by P Bhargava et al¹⁹ showed 96% sensitivity and 78.5% specificity for excision biopsy and our study showed sensitivity of 96.4% and specificity of 88.4% for excision biopsy.

CONCLUSION

This was a descriptive prospective analytical diagnostic study. This study was done for the comparative analysis of different diagnostic modalities available for diagnosis of tubercular cervical lymphadenitis and comparing them with excision biopsy, which is considered as the gold standard.

The laboratory diagnosis of tubercular lymphadenitis is generally established by histopathology (HPE), microscopic demonstration of Acid-Fast Bacilli (AFB) and mycobacterial culture of biopsy specimens. Each of these diagnostic

methods has its own merits and demerits and varies in terms of sensitivity and specificity. The presence of caseation necrosis and epithelioid cell granulomas is taken as diagnostic of tuberculosis on HPE. However, granulomatous lymphadenopathy has a wide differential diagnosis and many other clinical conditions can present the same cytology and histopathology as TB lymphadenitis. Demonstration of AFB by Ziehl-Neelsen (ZN) stain is simple and rapid, but lacks sensitivity. AFB culture on LJ media is sensitive and highly specific, but takes 4 to 12 weeks to give results.

It showed that biopsy is the best investigation for diagnosis of tubercular lymphadenopathy and have a high sensitivity and specificity, hence considered as a gold standard investigation for tubercular lymphadenitis. On comparison with other investigations like Mantoux, FNA culture on LJ medium, FNAC and ultrasonography, which are used for diagnosis of tubercular lymphadenopathy, ultrasonography showed high sensitivity followed by FNA culture on LJ medium, FNAC and Mantoux test, whereas on comparing specificity, FNA culture on LJ medium had a high specificity followed by Mantoux test, FNAC and ultrasonography.

To achieve a high specificity and sensitivity for diagnosis of tubercular lymphadenitis combination of two or more investigations can be used, but more studies are required to evaluate the optimal combination of these investigations for accurate and cost-effective analysis.

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