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Original Research Article

Reliability of FNAC as A Diagnostic Tool in Cases of Tuberculous Lymphadenopathy in Comparison with CBNAAT: Study Done at A Tertiary Care Center

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Abstract:

Introduction: Tuberculosis is one of the leading infectious causes of death worldwide wherein lymphadenopathy is the most frequent presentation of extra pulmonary tuberculosis. The usual site of presentation for EPTB lymphadenopathy is cervical region. Among various methods used to diagnose EPTB, conventional methods used are FNAC and ZN staining. The advanced methods used are CBNAAT, Truenat etc.

Objective: To assess the reliability of Fine Needle Aspiration Cytology (FNAC) over Cartridge Based Nucleic Acid Amplification Test (CBNAAT) for the diagnosis of Tuberculous lymphadenopathy.

Materials and Methods: The present retrospective study was conducted in the department of Pathology, Govt Medical College, and Ananthapuramu. It included all suspected Tuberculous Lymphadenopathy cases irrespective of age except for the cases which were already on treatment and those without CBNAAT/FNAC findings during the period from July 2022 to June 2023. Additionally, test reports of AFB staining, histopathology and culture were also noted.

Results: 117 cases in total with both FNAC and CBNAAT reports were analyzed, out of which 69 cases in FNAC showed features of either Granulomatous or necrotic smears and those were taken as positive. 71 cases in CBNAAT showed positive for tuberculosis. Composite reference standard was used for statistical comparison of FNAC and CBNAAT data which showed similar predictive Validity for both.

Conclusion: In areas where advanced techniques such as Gene expert are not readily available, easily accessible FNAC can be used as a primary diagnostic tool for EPTB lymphadenopathy cases. Even in centers with advanced diagnostic facilities, basic cytopathologic investigation must be combined with gene expert techniques to avoid false positive and false negative results.

Keywords: CBNAAT, Tuberculosis, FNAC, CRS.

Introduction

Tuberculosis is a serious and ancient epidemic that humans have known since time immemorial. As per the global TB report 2023, 10.6 million people fell ill with the disease worldwide in 2022. The incidence rate of disease was estimated to be increased by 1.9% between 2020-2021 and 2021-2022 [1]. Tuberculosis can affect people of all ages, and it has been rapidly escalating in developing countries like India in the past few decades [3].

According to India TB report 2023, in the year 2022, there was an increase of over 13% of TB case notifications [2]. Extra pulmonary tuberculosis (EPTB) is defined as per the World Health Organization as an infection by Mycobacterium tuberculosis that affects tissues and organs outside pulmonary parenchyma [4]. There are variable presentations for EPTB clinically, with lymphadenopathy being the most frequent one. The usual site of presentation for EPTB lymphadenopathy is cervical region. [5,6].

Due to the low bacterial count in the extra pulmonary manifestations of TB, it is necessary to conduct careful examination both clinically and microscopically along with ancillary techniques wherever available for the early diagnosis and treatment. EPTB is challenging to diagnose due to nonspecific/vague clinical symptoms. Routine investigations like chest radiography and sputum examination are not useful in these cases because

of probable lack of pulmonary infection. Conventional methods used for the diagnosis of EPTB are FNAC, AFB staining and culture. Despite being cost effective and more efficient, the lack of detection of rifampicin resistance by FNAC smear examination and the long duration of culture results make these investigations less preferred. WHO recommends technique of CBNAAT as a more sensitive and rapid diagnostic test for specimens from non-pulmonary sites [7] for the diagnosis of tuberculosis.

Lack of access to advanced diagnostic tests in small health centers and false positive/negative results from those advanced techniques due to many reasons like previous BCG vaccination, insufficient sampling etc. requires conventional methods like Fine needle aspiration cytology for better evaluation of the EPTB cases.

Objective:

To assess the reliability of FNAC over CBNAAT for the diagnosis of tuberculous lymphadenopathy.

Materials and Methods:

The present retrospective study was conducted in the department of Pathology, Govt Medical College, and Ananthapuramu and comprised all cases of clinically suspected tuberculous lymphadenopathy, regardless of age, that occurred between July 2022 and June 2023.

Data pertaining to FNAC, CBNAAT reports, and clinico-radiological information were considered. In addition to these, AFB staining, histopathology, and culture reports were also gathered.

Cases already on treatment and cases without either FNAC or CBNAAT report were excluded from the study. FNAC procedure was performed with 20-22 gauge needles and the aspirate taken on to the slide was stained with H & E, also AFB staining in cases of suspicion. Smears were examined under the microscope. Aspiration from FNAC was sent to CBNAAT and culture which reported as either positive or negative. The biopsy sample sent for histopathology was fixed with formalin, processed, embedded, cut, and finally stained with H & E after taking the tissue on to a slide.

Results

A total of 117 suspected tuberculous lymphadenopathy cases were studied from the recorded data for which both FNAC and CBNAAT findings were available along with histopathology and culture reports in cases where additional confirmation was required. Clinical presentation in all the above cases except for the feature of lymphadenopathy was very vague with only few showing symptoms like evening rise of temperature, weight loss etc. The mean age recorded was between 20 and 30 years with the youngest age reported in our case being 2 years child and the maximum age reported was 51 years. Females were found to be dominant in the current study with male to female ratio being 1:1.12.

Among various sites of presentation, cervical region was the commonest accounting for 84% followed by axillary, inguinal and supraclavicular with 8.5%, 5% and 2.5% respectively. 81 cases showed solitary swelling whereas the remaining cases showed multiple lymphadenopathies.

Cytological patterns encountered in the FNAC were Granulomatous lymphadenitis with or without necrosis, occasional epithelioid with necrosis , only necrosis, reactive lymphadenitis, suppurative lymphadenitis. The first 4 patterns had AFB staining done to confirm Koch's etiology and all those cases were taken as positive in FNAC accounting for 69/117 cases. Remaining cases were categorized as reactive accounting for 28% (32) and suppurative accounting for 13.6% (16 cases) All 117 cases were sent for CBNAAT in which 71 were found to be positive for tuberculosis. Among 69 positive cases of FNAC, CBNAAT showed positivity for 63 and 6 cases were negative. Among 48 negative cases of FNAC, 8 were positive in CBNAAT for tuberculosis.

Same cases were received in histopathology as either biopsy or excision specimen and samples from FNAC were sent to culture in addition to CBNAAT for confirmation. A composite Reference Standard was defined by the combined results of histopathology and culture along with FNAC and CBNAAT. In the total of 117, CRS showed positivity in 74 and negative in 43 for tuberculosis.

Though CBNAAT is considered the gold standard, there are many situations where it showed false positive and false negative results. Therefore, in the present study, a composite reference standard (CRS) was taken to compare the results of both FNAC and CBNAAT. Initially, FNAC data was compared with CBNAAT, result showed sensitivity of 88.7%, Specificity of 86.9%, positive predictive value of 91.3%, negative predictive value of 83.3% and diagnostic accuracy of 88% for FNAC.

Then the data of FNAC was compared with the CRS which yielded a sensitivity of 91.8%, specificity of 97.6%, positive predictive value of 98.5% , negative predictive value of 87.5%, diagnostic accuracy of 94.2% Chi square test was performed which showed a score of 90.174 with p value significant at $p<0.01$ Then the data of CBNAAT was compared with CRS which yielded a sensitivity of 93.2%, Specificity of 95.3%, positive predictive value of 97.1%, negative predictive value of 89.13% and a diagnostic accuracy of 94.02%. Chi square test was performed

which showed a score of 89.465 with P value significant at p<0.01.

Table 1: Sex wise distribution

	Number of cases	Percentage
Male	55	47
Female	62	53

Table 2: Site wise distribution

Site	Number of cases	Percentage (%)
Cervical	98	84
Axillary	10	8.5
Inguinal	6	5
Supraclavicular	3	2.5

Table 3: Cytological pattern

FNAC pattern	Number of cases	Percentage (%)
Well defined granulomas without necrosis	33	28.3%
Well defined granulomas with necrosis	18	15.3
Occasional epithelioid with necrosis	5	4.2%
Only caseous necrosis	13	11.1%
Reactive	32	27.4%
Suppurative	16	13.7%
Total	**117**	

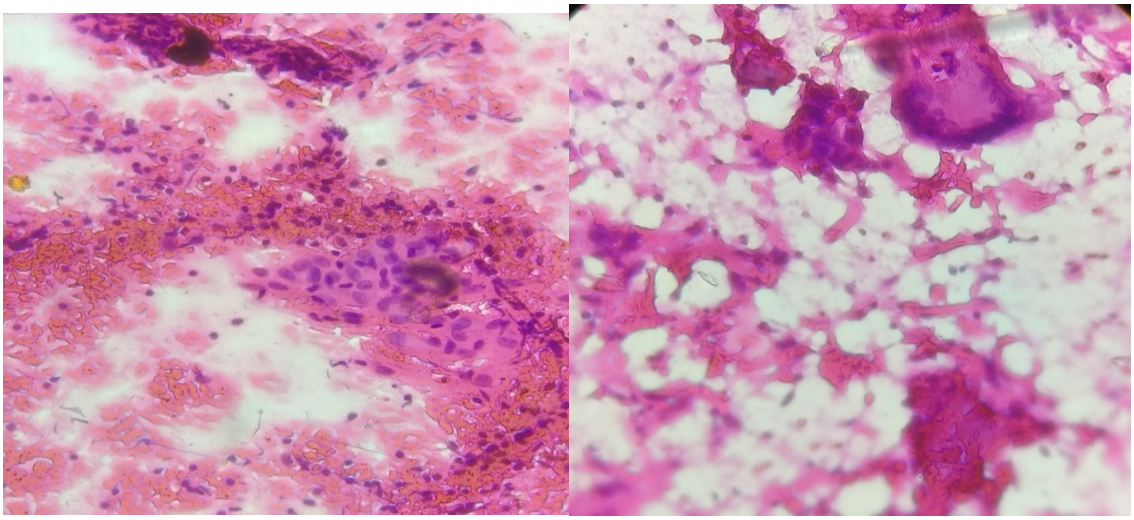

Figure 1 & 2: H & E stained Images 1,2 - Epithelioid granuloma and Langhans type of giant cell

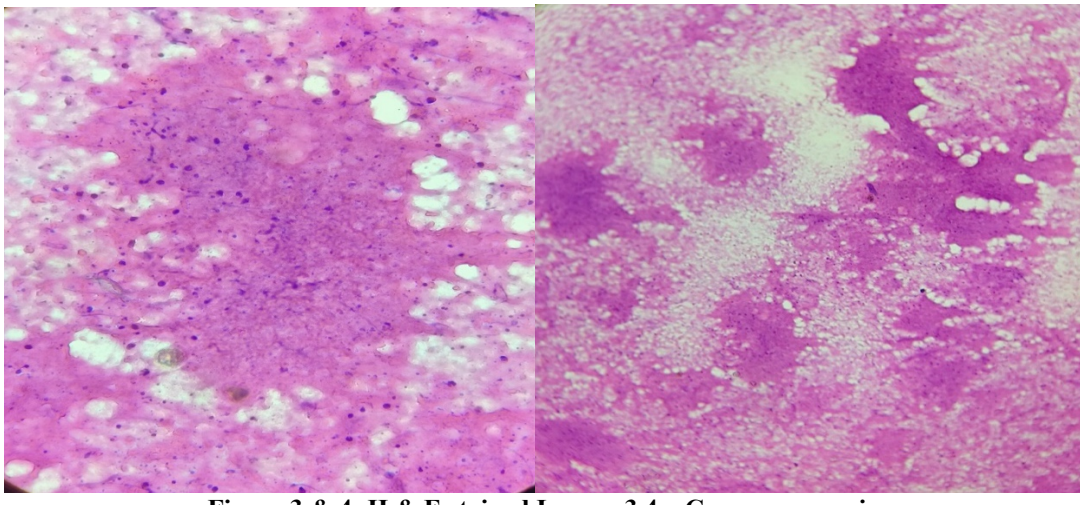

Figure 3 & 4: H & E stained Images 3,4 – Caseous necrosis

Limitations:

1. Small sample size
2. Single center study
3. As it was a retrospective study, data available for collaboration and correlation was limited.

Discussion:

India accounted for 27% of global burden with 2.8 million cases reported in the year 20221. Although lungs are the most typically affected site in TB (pulmonary TB), organ systems other than the lungs can also be affected. According to The Global TB Report 2020, extra pulmonary tuberculosis (EPTB) constituted 16% of the 7.5 million reported TB cases globally and 19% in South-East Asia [16].

However, these estimates may be the tip of the iceberg, as a considerable proportion remains undiagnosed or not notified hence there is a need for diagnostic progress along with the therapeutic development.

Present study showed mean age group to be 26 years which is concordant with Manju et al [10], Kalyani Gouda et al [13].

Female predominance in the current study is concordant with the study Chaudhari et al [19], Kalyani Gouda et al [13]. Unilateral lymph node presentation was the most seen presentation in the current study, which is consistent with Shilpa g et al [14].

In the distribution of various sites of presentation, cervical was the most common region in our study, concordant with /Shilpa et al [14].

Cytological criteria taken into consideration for the diagnosis of tuberculosis in the current study were Epithelioid granulomas, Langhans type giant cells with or without caseous necrosis and ZN staining positivity in the absence of necrosis similar to other studies [8,9,11].

Comparing the cytological pattern with other studies, present study showed granulomas without necrosis in 28.3% which is concordant with Dhote et al [20]., pattern showing occasional epithelioid was seen in 4.2% in the present study which is concordant with Dhote et al [20]., Percentage of cases showing only necrosis in the present study was 11.1% which is nearly concordant with all the compared studies.

Total sample positivity in the present study taking CRS as standard with FNAC is 93%, with CBNAAT is 95%. Overall, in the suspected tuberculous lymphadenopathy cases, the percentage of positivity for FNAC is 58.9% and CBNAAT is 60.6%. Improper collection and transportation may result in false results of CBNAAT (Massoud et al [30]).

Table 4: Comparison of Cytological pattern with other studies:

Pattern	Present study (%)	Adhikary et al [17]	Shilpa G et al [14]	Chaudhari et al [19]	Dhote et al [20]
Granulomas without necrosis	28.3%	15.2%	51.2%	48.8%	25%
Granulomas with necrosis	15.3	38%	34.2%	59%	29%
Occasional epithelioid with necrosis	4.2%	-	-		3.4%
Only necrosis	11.1%	17.7%	14.6%	37.5%	16%

Table 5: FNAC Predictive validity

Parameter	Present study	Chaudhari et al [19]	Siddegouda et al [16]	Sellami M et al [21]	Manju et al [10]
Sensitivity	91.8%	94.3%	85.7%	83.3%	53.85%
Specificity	97.6%	87.1%	73.8%	83.3	90.48%
PPV	98.5%	18.3%	63.8%	78.9%	91.3%
NPV	87.5%	99.8%	90.5%	86.9%	51.35%
Diagnostic accuracy	94.2%	87.3%	78%	-	-

Predictive validity of FNAC in our study showed sensitivity of 91.8%, concordant with Chaudhary et al [19], Siddegouda et al [16] and Sellami M et al. [21] but Manju et al. [10] showed sensitivity of 53.85%. Specificity of 97.6% was seen in the current study, which was concordant with Chaudhari et al and Sellami M et al. [21] PPV of 98.5% seen in the current study was concordant with Manju et al. [10] and NPV was concordant with Siddegouda et al. [16] study.

Table 6: CBNAAT predictive validity comparison

Parameter	Present study	Divya et al [11]	K Arpitha et al [18]	Shilpa G et al [14]	Manju et al [10]
Sensitivity	93.2%	84.61%	80%	37%	79.49%
Specificity	95.3%	39.72%	85.4%	80%	100%
PPV	97.1%	93.54%	65%	76.9%	100%
NPV	89.1%	20%	45.5%	41.38%	72.41%
Diagnostic accuracy	94.02%			52.38%	

CBNAAT predictive validity in the current study showed sensitivity of 93.2% concordant with Divya et al. [11] and K Arpitha et al. [18] whereas Shilpa G et al. [14].

Study showed only 37% sensitivity. Specificity in this study is concordant with all the compared studies except Divya et al study which showed only 39.7%.

Conclusion

FNAC is an inexpensive, easily accessible, nonhazardous, and reliable investigation in the diagnosis of tuberculous lymphadenopathy. CBNAAT is a rapid investigation and offers resistance estimation to Rifampicin; it can be combined with FNAC in addition to other ancillary techniques like ZN staining for accurate results.

Table 7: List of abbreviations

S.no	Abbreviation	Full form
1	CBNAAT	Cartridge Based Nucleic Acid Amplification Test
2	ZN	Ziehl-Neelsen
3	EPTB	Extra pulmonary tuberculosis
4	TB	Tuberculosis
5	AFB	Acid Fast Bacilli
6	FNAC	Fine needle Aspiration Cytology
7	CRS	Composite Reference Standard

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