

Study of Serum Adenosine Deaminase (ADA) Level in FNAC Confirmed Cases of Tubercular Lymphadenitis

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Abstract

Background: Tuberculosis is a chronic pulmonary and systemic disease that predominantly occurs due to *Mycobacterium tuberculosis* infection. TB is a leading health hazard globally. Tubercular lymphadenitis is the commonest type of presentation of extrapulmonary TB. The Present study was done to assess correlation between FNAC and serum ADA level in diagnosing tubercular lymphadenitis and to rule out early tuberculosis in cases reported as reactive lymphadenitis by FNAC.

Materials and Methods: A two-year prospective study of 54 cases of clinically suspected tubercular lymphadenitis from December 2020 to November 2022 was done. The study subjects were first confirmed by FNAC along with AFB staining. This was followed by measurement of serum ADA levels.

Results: The mean age of the patients in this study was 29 years with slight predilection for female sex. Only 24%, 13 cases present with constitutional symptoms. In cytomorphology 22 cases (40.74%) diagnosed as granulomatous lymphadenitis, while 2 cases diagnosed as reactive lymphadenitis only. Most of cases (39 cases, 72.2%) show significant increase in serum ADA level.

Conclusions: FNAC along with raised serum ADA level can be considered as a reliable indicator of tubercular lymphadenitis and is fairly significant though demonstration of AFB Ziehl-Neelsen stain is gold standard.

Keywords: Tuberculosis, FNAC, ADA.

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Introduction

Tuberculosis is a chronic pulmonary and systemic disease, predominantly occurred due to *Mycobacterium tuberculosis* infection.. TB is a leading health hazard in the world.[1] Although TB is a known infectious

disease with a definite epidemiological pattern and known principles of treatment, yet there is a considerable number of TB patients in many parts of the world. [2] In healthy people, infection with M.

tuberculosis often causes no symptoms, as the person's immune system acts to "wall off" the bacteria.

M. tuberculosis infection may produce granulomas consisting of epithelioid histiocytes. Langhan's type of giant cells and caseating necrosis can be seen along with it. But in some cases it may produce only caseous necrosis. Atypical cases of FNAC confirmed TB will show low to moderate cellularity, presence of epithelioid histiocytes in the form of granulomas, multinucleated giant cells with irregularly arranged nuclei that may aggregate or be peripherally arranged in horse-shoe in the granular or finely vacuolated, pale cytoplasm (Langhan's giant cells).[4]

The demonstration of an AFB is diagnostic of Tuberculosis. A sample is called 'diagnostic' when Ziehl-Neelsen stain and/or culture is positive, 'suggestive' when there is granulomatous inflammation and 'inconclusive' when there is non-specific inflammation or isolated giant cells or blood components.[5]

Adenosine deaminase (ADA) is an enzyme released by monocytes/macrophages that contributes in purine metabolism and transforms adenosine and deoxyadenosine to inosine and deoxyinosine [6]. The increase serum level of ADA has been reported for viral and bacterial pneumonia, for HIV infection and extrapulmonary Tuberculosis.[7] Level of ADA in body fluids especially pleural fluid has proven to be highly sensitive and specific for diagnosis of extra-pulmonary tuberculosis [8]. Activity of ADA increases when T lymphocytes are stimulated by mycobacterium. The importance of ADA in body fluids has already been established for the diagnosis of pleural and other extrapulmonary tuberculosis, where sputum often leads to inconclusive result [9].

A quick way to detect M. tuberculosis infection will help speed up early diagnosis in clinically suspected patients with tuberculosis and prompt follow-up of management.[10] Therefore, this study was done to assess correlation between FNAC and serum ADA level in diagnosing tubercular lymphadenitis and to rule out early tuberculosis in cases reported as reactive lymphadenitis by FNAC.

Materials and Methods

54 cases of clinically suspected tuberculous lymphadenitis attended the outpatient department, underwent FNAC in the Pathology Department, M.G.M Medical College & LSK Hospital, Kishanganj, Bihar. After obtaining approval and clearance from the institution, ethical committee, patients was included for study. Patients with known cases of heart disease, liver disease, lymphocytic lymphoma, Q fever & other causes of increase serum ADA levels other than tuberculosis were excluded from the study.

Methodology

The subjects first diagnosed by Fine needle aspiration cytology and AFB staining. This was followed by measurement of serum ADA level. FNAC was performed in all cases using 23G needle and 10cc syringe, the material aspirated on FNA was used to make the smears. Air dried smears were stained immediately with Giemsa stain for cytomorphological study and ZN stain for AFB.

Statistical Methods

We employed descriptive and inferential statistical analyses and the convenience sampling method applied to recruit consecutive patients who satisfied the inclusion criteria.

The following formula was employed for computing the sample size of the present

study at a 95% confidence level, which was calculated from the formula below.

- $n = z^2 \times p \times q / \alpha^2$
- where, n = the sample size, z = the standard normal deviation equivalent to 95% level of confidence = 1.96, α = allowable error = 5% (0.05), p = prevalence = 5%
- n \approx 73, But due to COVID 19 scenario, we got 54 cases only. Significance was assessed at 5% level of significance by

applying Student t test and Chi-square test.

Results

The majority of cases, 30 (56%) were \leq 30 years old, followed by 13(24%) cases between 31 – 45 years old, 8 (14%) cases between 45 – 60 years old, and 3 (6%) over 60 years old. While the mean age of patients was 29 years. Out of 54 samples, 31 (58%) cases were female and 23 (42%) were males, showing female predominance.

Table 1: Distribution of cases according to age

Age Group (Years)	No.
\geq 30	30(56%)
31-45	13(24%)
46-60	8(14%)
\geq 61	3(6%)

Table 2: Distribution of cases according to gender

Gender	No.
Female	31 (58%)
Male	23 (42%)

13 (24%) cases showed constitutional symptoms while others 41(76%) presented without such symptoms. In cytomorphology 22 cases (40.74%) diagnosed as granulomatous lymphadenitis, while 2 cases diagnosed as reactive lymphadenitis only.

Table 3: Clinical findings of the cases

Clinical findings	No.
Swelling with or without fever	41(76%)
Swelling with Fever & Loss of weight	13(24%)

Table 4: Nature of cytomorphology

Cytomorphology	AFB Positive
Necrosis with Lymphocytes	20
Necrosis with granuloma	22
Necrosis without granuloma	10
Reactive lymphoid cells with nonspecific inflammation	2

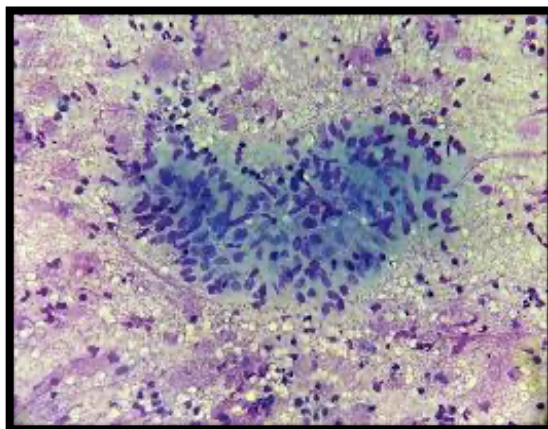
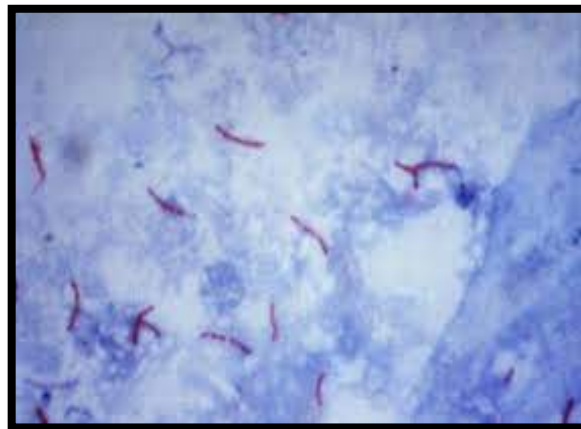
Most of cases (39 cases, 72.2%) show significant increase in serum ADA level.

Table 5: Relationship between serum ADA and cytologically confirmed tuberculosis

Serum ADA Level	No.	Percentage %
Normal	15	27.8%
High	39	72.2%

Table 6: Relationship between serum ADA level and cytomorphology of Tuberculosis

Cytomorphology	AFB Positive	ADA Positive	ADA Negative	P value
Necrosis with granuloma	22	21	1	0.028534
Necrosis without granuloma	10	8	2	
Necrosis with lymphocytes	20	9	11	
Reactive lymphoid cells with non-specific inflammation	2	1	1	

**Figure 1: Photomicrograph showing granuloma, 40x(H&E Stain)****Figure 2: Photomicrograph showing rod shaped acid fast bacilli in ZN stain, 100x**

Discussion

Tuberculosis is a leading health hazard in the world . Prompt diagnosis and treatment are important aspect of the evaluating tuberculosis [11]. Diagnosis of Tuberculosis is depended on clinical as well as radiological findings along with detection of acid fast bacilli in sputum smear. Sometimes clinical and radiological findings can vary which may

appear as false negative [12]. Thus, it is essential to perform some rapid and useful tests for the detection of tuberculosis[13].

Measurement of serum adenosine deaminase (ADA) level in body fluids is a valuable marker for tuberculosis [14]. Multiple studies also indicated that the serum levels of ADA

significantly higher in pulmonary TB than other respiratory diseases like lung cancer, chronic obstructive pulmonary disease, pneumonia [15].

The present study showed maximum of cases 30 (56%) were ≤ 30 years, which is similar by a study done by Mugulkod P *et al* [16], where the most common age group affected by extra pulmonary tuberculosis was 3rd and 4th decade. In our study, out of 54 samples, 31 (58%) cases were female and remaining 23 (42%) were males, showing female predominance, which is comparable with the study done by Ina Garg *et al* [17].

In the current study, 20 cases were necrosis with lymphocytes, 22 cases were epithelioid cell granulomas with caseous necrosis, 10 cases were epithelioid cell granuloma without caseous necrosis, and 2 cases were reactive lymphoid cells with nonspecific inflammation. Similar results were observed studies done by Das DK *et al* [4] and Radhika S *et al* [18].

In our study it is found that 39 cases (72.2%) out of 54 cases found to be elevated and about 27.8% cases were found to be normal ADA level. In this study, serum ADA level was found to be significantly high in patients with tuberculosis (P value is .028534, which is significant at $P < .05$). A study done by Agarwal M *et al* also showed similar result [19].

Studies done by Verma M *et al* [20] and Jhamaria JP *et al* [21], further showed a significant higher mean difference of serum ADA levels between pulmonary TB and others respiratory diseases with a statistically significant raised in serum ADA values in pulmonary TB.

Conclusion

FNAC is reliable, quick and economical investigating modality in tubercular lymphadenitis. Despite certain limitations and pitfall it provides a high degree of

accuracy in diagnosing tubercular lymphadenitis. The raised serum ADA level can be considered as a reliable indicator of tubercular lymphadenitis and is fairly significant though demonstration of AFB Ziehl-Neelsen stain is gold standard.

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