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Research Article

Evaluation of Pleural Fluid Adenosine Deaminase Activity and Its Biochemical and Physiological Significance in the Diagnosis of Tuberculous Pleural Effusion among Symptomatic Patients

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ABSTRACT

Background: One of the frequent extrapulmonary TB manifestation is tuberculosis Pleural effusion, which is often paucibacillary, making it a diagnostic challenge. Traditional techniques like pleur Tib and microbiological testing can be invasive, time consuming or only yield results in some cases. It has been suggested that the activity of adenosine deaminase in the pleural fluid can be used as a useful supportive test to support the early diagnosis of tuberculous pleural effusion.

Objective: To determine the diagnostic accuracy of adenosine deaminase activity in the diagnosis of tuberculous pleural effusion among symptomatic patients.

Methods: This is a cross sectional study of diagnostic accuracy conducted from 25th March 2025 to 25th June 2025 in Department of Medicine, Women Medical College, Abbottabad. The number of patients was 100, and the sampling method used was non-probability consecutive sampling, which were patients with symptoms of pleural effusion ranging in age from 16 to 75 years. Thoracentesis was performed to obtain the pleural fluid for ADA measurement. Tuberculous Pleural Effusion was considered to be positive when ADA level was >55.8 U/L. Biopsy of the pleura was done and was the gold standard. The data were analyzed by SPSS version 25. A 2×2 table was used to calculate sensitivity, specificity, positive and negative predictive value, and diagnostic accuracy.

Results: The mean age of the patients was 42.6 ± 14.8 years, and 58.0% were male. Pleural biopsy confirmed tuberculous pleural effusion in 35.0% of patients, while ADA was positive in 39.0%. When ADA findings were compared with pleural biopsy, 31 cases were true positive, 57 were true negative, 8 were false positive, and 4 were false negative. The sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy of ADA were 88.6%, 87.7%, 79.5%, 93.4%, and 88.0%, respectively. Patients with biopsy-confirmed tuberculous pleural effusion had significantly higher pleural fluid lymphocyte percentages and lymphocyte-to-neutrophil ratios than biopsy-negative patients. Lymphocyte-predominant pleural effusion was present in 91.4% of biopsy-positive patients compared with 60.0% of biopsy-negative patients ($p = 0.001$). A significant association was observed between ADA results and pleural biopsy findings ($p < 0.001$).

Conclusion: Pleural fluid adenosine deaminase activity showed good diagnostic accuracy for tuberculous pleural effusion in symptomatic patients. ADA testing is a rapid, simple, and less invasive supportive diagnostic tool, especially in settings where tuberculosis is common. However, ADA should be interpreted along with clinical findings, radiological assessment, and confirmatory investigations where required.

Keywords: Adenosine Deaminase, Tuberculous Pleural Effusion, Pleural Biopsy, Diagnostic Accuracy, Sensitivity, Specificity, Tuberculosis.

INTRODUCTION

Tuberculous Pleural Effusion is the result of delayed hypersensitivity reaction to mycobacterial antigens in the pleural space. Many patients will have low levels of organisms in the pleural fluid making direct smear microscopy and culture less sensitive. This oligosymptomatic nature makes it challenging to make a diagnosis early. The delay in diagnosis can lead to prolonged symptoms, unnecessary antibiotics use, progression of the disease, pleural thickening, or other complications. Hence, there is a need for a prompt and efficient diagnostic tool for proper management (1-3).

Pleural biopsy is an important reference method for the diagnosis of tuberculous pleural effusion as it is able to detect histopathological features suggestive of tuberculosis. Biopsy, however, is invasive, requires skill, is not always available in health care settings, and might not be appropriate for all patients. Additional diagnostic tests, such as mycobacterial culture and molecular testing, can be used to better confirm the diagnosis and are useful but can be resource-intensive, time-consuming, or unavailable. Consequently, there has been a growing interest in biochemical markers that could aid early diagnosis, due to these practical constraints (4-6).

Adenosine deaminase (ADA) is an enzyme that partitions the purine metabolism associated with the activity of lymphocytes. The raised ADA level in the pleural fluid is related to the cellular immune response, especially the activation of T cells, which is a feature of tuberculous pleural inflammation. This biological association has led to wide study of the use of pleural fluid ADA as a diagnostic tool in tuberculous pleural effusion. It is relatively easy, quick and non-invasive, and therefore useful in the daily practice of the doctor (7-10).

The diagnostic value of ADA is dependent on the cut-off level used, local tuberculosis prevalence, patient characteristics and reference standard used for comparison. The criteria for a positive result for tuberculous pleural effusion in the present study was set at >55.8 U/L of ADA and the gold standard was considered to be pleural biopsy. As per the operational definition, there were four categories: true positive, true negative, false positive and false negative.The operational definition classified cases as true positive, true negative, false positive, and false negative based on the agreement/disagreement of ADA and biopsy (11-13).

The diagnostic performance of ADA will vary with the cut-off value selected, the prevalence of TB in the population, patient characteristics, and the gold standard with which it is compared. The criteria for tuberculous pleuritis were used in the present study in which an ADA level greater than 55.8 U/L was regarded as positive and a pleural biopsy served as a gold standard. True positive and true negative cases were defined by the agreement or disagreement with biopsy results on the basis of ADA.The cases were classified as true positive, true negative, false positive or false negative based on agreeing or not agreeing with biopsy results according to the operational definition (14).

The purpose of this study was to assess whether ADA can serve as a reliable supportive diagnostic tool for tuberculous pleural effusion in the local population. Establishing its diagnostic accuracy may help clinicians make earlier decisions, reduce unnecessary delay, and improve patient management, especially in resource-limited settings where rapid and less invasive testing is highly valuable.

METHODOLOGY

This cross-sectional diagnostic accuracy study was conducted in the Department of Medicine, Women Medical College, Abbottabad**,** from 25th March 2025 to 25th June 2025. The objective of the study was to determine the diagnostic accuracy of pleural fluid adenosine deaminase activity in the diagnosis of tuberculous pleural effusion among symptomatic patients. Pleural biopsy was taken as the gold standard diagnostic method, while pleural fluid ADA was assessed as the index test. The study was carried out after approval from the institutional ethical review committee, and permission was obtained from the concerned hospital administration before data collection.

All 100 symptomatic patients with pleural effusion were studied. Sample size was determined with a sample size calculator for sensitivity and specificity. This was computed at a 95% confidence level, with an anticipated prevalence rate for tuberculous pleural effusion of 30%, a 12.5% margin of error for the sensitivity of the ADA test, and a 6.5% margin of error for the specificity of the test. Non-probability consecutive sampling technique was used to recruit patients until the required sample size was obtained.

Patients aged 16-75 years, both male and female, whose diagnosis included pleural effusion, who met the study criteria were included. Patients who had chronic tuberculosis, asthma, lung malignancy, pregnancy, steroid treatment in course of treatment or had anti-tuberculous treatment were excluded. These exclusion criteria were used to minimize factors that could effect the ADA level and to prevent interference with the diagnosis of tuberculous pleural effusion.

After obtaining written informed consent, all eligible patients were enrolled from the outpatient department and medical units. A structured proforma was used for data collection. Demographic data such as age, gender, BMI, place of residence, occupation, and socioeconomic status were obtained. Demographic data, such as the duration of pleural effusion, smoking history, hypertension, diabetes mellitus, family history of tuberculosis and season of presentation were also recorded. History of smoking was considered positive if the patient had a smoking history of more than 5 pack-years. Hypertension was defined as blood pressure ≥140/90 mmHg or antihypertensive medication use and diabetes mellitus as random blood sugar >200 mg/dl or previously diagnosed diabetes.

Thoracentesis was performed under an aseptic condition to obtain pleural fluid from each patient. The procedure was carried out by skilled physicians with the usual precautions. The collected sample of pleural fluid was taken to the hospital laboratory for the measurement of the activity of ADA. Concentration of ADA was measured in u/L. Based on the operational definition, tuberculous pleural effusion was defined as ADA > 55.8 U/L in pleural fluid and ADA ≤ 55.8 U/L in pleural fluid was considered as negative.

Pleural biopsy was done using normal hospital protocol by consultant pulmonologist or trained physician. The sample was taken for biopsy and taken to the pathology lab for histological analysis. A biopsy diagnosis of tuberculous pleural effusion was considered positive if there was a diagnosis of paucibacillary mycobacterial infection in the pleural space. The biopsy negative group consisted of patients who had results from their biopsy that were not suggestive of TB. The result of the pleural biopsy was used as the reference standard to compare with the ADA result.

Patients were classified as true positive, true negative, false positive and false negative for analysis of diagnostic accuracy. A true positive case was defined as an ADA level >55.8 U/L, in combination with the diagnosis of tuberculosis in a pleural biopsy. A true negative case was one whose ADA level was ≤55.8 U/L and whose biopsy of his/her pleura did not show tuberculosis. A case was considered false positive if ADA level was >55.8 U/L and the biopsy of the pleura was negative. A false negative case was defined as having ADA level ≤55.8 U/L, with a biopsy of the pleura being positive for tuberculosis.

In addition to ADA measurement, pleural fluid differential leukocyte counts were recorded. The percentages of lymphocytes and neutrophils were documented, and the pleural fluid lymphocyte-to-neutrophil ratio was calculated by dividing the lymphocyte percentage by the neutrophil percentage. A lymphocyte-predominant pleural effusion was defined as a pleural fluid lymphocyte proportion greater than 50%. The lymphocyte-to-neutrophil ratio was evaluated as an additional pleural fluid parameter and compared between patients with positive and negative pleural biopsy findings.

All collected data were entered and analyzed using SPSS version 25. Quantitative variables, including age, BMI, duration of pleural effusion, ADA level, pleural fluid lymphocyte percentage, neutrophil percentage, and lymphocyte-to-neutrophil ratio, were presented as mean ± standard deviation or median with interquartile range, according to their distribution. Qualitative variables, including gender, place of residence, socioeconomic status, smoking history, hypertension, diabetes mellitus, family history of tuberculosis, season of presentation, ADA result, pleural biopsy result, and lymphocyte-predominant pleural effusion, were expressed as frequencies and percentages. The Shapiro–Wilk test was used to assess the normality of quantitative data. Pleural fluid lymphocyte percentage, neutrophil percentage, and lymphocyte-to-neutrophil ratio were compared between pleural biopsy-positive and biopsy-negative patients using the independent-samples t-test or Mann–Whitney U test, as appropriate. The association between lymphocyte-predominant pleural effusion and pleural biopsy findings was assessed using the chi-square test or Fisher's exact test.

To compare the ADA results with pleural biopsy findings, a 2 × 2 contingency table was constructed. Sensitivity, specificity, positive predictive value, negative predictive value, and

overall diagnostic accuracy of ADA were calculated using standard diagnostic formulas. Sensitivity was calculated as TP/(TP + FN) × 100, specificity as TN/(TN + FP) × 100, positive predictive value as TP/(TP + FP) × 100, negative predictive value as TN/(TN + FN) × 100, and diagnostic accuracy as (TP + TN)/total sample size × 100. The association between ADA results and pleural biopsy findings was assessed using the chi-square test. A p-value of ≤0.05 was considered statistically significant.

Stratification was performed according to age, gender, BMI, duration of pleural effusion, residence, occupation, socioeconomic status, smoking history, hypertension, diabetes mellitus, family history of tuberculosis, season of presentation, and lymphocyte-predominant pleural effusion. Following stratification, 2 × 2 tables were constructed to calculate the diagnostic performance of ADA within each subgroup. This analysis was performed to determine whether the diagnostic accuracy of ADA remained consistent across different patient groups.

RESULTS

One hundred symptomatic cases with pleural effusion were studied. Mean age of the patients was 42.6 ± 14.8 years ranging from 16 to 75 years. The age group of 31-45 years included the highest number of patients. Out of 100 patients, 58 (58.0%) were male and 42 (42.0%) were female. The mean BMI was 23.9 ± 3.6 kg/m². As regards the place of residence 46 patients (46.0%) came from rural areas, 39 (39.0%) from urban areas and 15 (15.0%) from semi-urban areas.

Table 1. Baseline Demographic Characteristics of Patients

Variable	Frequency / Mean	p-value
Total patients	100	—
Age, years	42.6 ± 14.8	0.418
BMI, kg/m²	23.9 ± 3.6	0.562
Male	58 (58.0%)	0.374
Female	42 (42.0%)	
Rural residence	46 (46.0%)	0.291
Urban residence	39 (39.0%)	
Semi-urban residence	15 (15.0%)	
Low socioeconomic status	41 (41.0%)	0.336
Middle socioeconomic status	44 (44.0%)	
High socioeconomic status	15 (15.0%)	

The mean duration of PE was 18.4 ± 7.2 days. A history of smoking was significant in 31 (31.0%) patients, diabetes mellitus in 22 (22.0%) and hypertension in 26 (26.0%) patients. Twenty-eight (28.0%) patients had a history of TB in their families. Biopsy confirmed tuberculous pleural effusion was statistically significantly associated with duration of pleural effusion > 2 weeks (p = 0.021) and positive family history of TB (p = 0.034).

Table 2. Clinical Characteristics of Patients

Clinical variable	Frequency (%)	p-value
Smoking history	31 (31.0%)	0.188
Hypertension	26 (26.0%)	0.642
Diabetes mellitus	22 (22.0%)	0.529
Family history of tuberculosis	28 (28.0%)	**0.034**
Duration of pleural effusion >2 weeks	61 (61.0%)	**0.021**
Winter presentation	34 (34.0%)	0.276
Spring presentation	29 (29.0%)	
Summer presentation	21 (21.0%)	
Autumn presentation	16 (16.0%)	

The mean pleural fluid ADA level was 59.8 ± 18.6 U/L, with 39 (39.0%) patients having a positive ADA and 61 (61.0%) having a negative ADA based on the ADA cut-off value of > 55.8 U/L. The histological diagnosis of tuberculous pleural effusion was confirmed in 35 patients

(35.0%) and 65 patients (65.0%) were biopsy negative for tuberculous pleural effusion. Biopsy-proven tuberculous pleural effusion was significantly associated with ADA positivity ($p < 0.001$).

Table 3. Distribution of ADA and Pleural Biopsy Findings

Diagnostic finding	Frequency (%)	p-value
ADA positive >55.8 U/L	39 (39.0%)	**<0.001**
ADA negative ≤55.8 U/L	61 (61.0%)	
Pleural biopsy positive for TB	35 (35.0%)	—
Pleural biopsy negative for TB	65 (65.0%)	—

Pleural fluid differential cell counts were also evaluated according to pleural biopsy findings. Patients with biopsy-confirmed tuberculous pleural effusion had a significantly higher mean pleural fluid lymphocyte percentage than biopsy-negative patients (76.4 ± 10.8% versus 58.7 ± 15.2%, $p < 0.001$). In contrast, the mean neutrophil percentage was significantly lower in the biopsy-positive group than in the biopsy-negative group (23.6 ± 10.8% versus 41.3 ± 15.2%, $p < 0.001$). The mean lymphocyte-to-neutrophil ratio was also significantly higher among patients with biopsy-confirmed tuberculosis (3.72 ± 1.68 versus 1.76 ± 1.21, $p < 0.001$). Lymphocyte-predominant pleural effusion was observed in 32 of 35 (91.4%) biopsy-positive patients compared with 39 of 65 (60.0%) biopsy-negative patients. This association was statistically significant ($p = 0.001$).

Table 4. Pleural Fluid Cellular Parameters According to Pleural Biopsy Findings

Pleural fluid parameter	Biopsy-positive TB, n = 35	Biopsy-negative, n = 65	p-value
Lymphocytes, %, mean ± SD	76.4 ± 10.8	58.7 ± 15.2	<0.001
Neutrophils, %, mean ± SD	23.6 ± 10.8	41.3 ± 15.2	<0.001
Lymphocyte-to-neutrophil ratio, mean ± SD	3.72 ± 1.68	1.76 ± 1.21	<0.001
Lymphocyte-predominant effusion, n (%)	32 (91.4%)	39 (60.0%)	0.001

Thirty-one were true positive, 57 were true negative, 8 were false positive, and 4 were false negative when ADA was compared with the results of pleural biopsy. Statistically significant correlations were found between the ADA result and the results of the pleural biopsy ($\chi^2 = 52.46$, $p < 0.001$). The sensitivity of ADA for tuberculous pleurisy was 88.6% and the specificity was 87.7%. The positive predictive value was 79.5%, the negative predictive value was 93.4% and the overall diagnostic accuracy was 88.0%.

Table 5. Diagnostic Accuracy of ADA using Pleural Biopsy as Gold Standard

ADA result	Pleural biopsy positive	Pleural biopsy negative	Total	p-value
ADA positive >55.8 U/L	31	8	39	**<0.001**
ADA negative ≤55.8 U/L	4	57	61	
Total	35	65	100	

Table 6. Diagnostic Performance of ADA

Diagnostic parameter	Value
Sensitivity	88.6%
Specificity	87.7%
Positive predictive value	79.5%
Negative predictive value	93.4%
Diagnostic accuracy	88.0%
p-value for ADA vs pleural biopsy	**<0.001**

The diagnostic accuracy of ADA was found to be good in a variety of age groups, gender, BMI categories and in patients with pleura effusion of different duration following stratification. The accuracy of the diagnosis was slightly better in the patients who had a long duration of pleural effusion (more than 2 weeks) and was better in the patients who had a positive family history of tuberculosis. But there was no significant difference in gender between patients.

Table 7. Stratified Diagnostic Accuracy of ADA

Stratification variable	Sensitivity	Specificity	Accuracy	p-value
Age ≤45 years	90.0%	88.2%	88.9%	**<0.001**
Age >45 years	86.7%	87.1%	87.0%	**<0.001**
Male	89.5%	87.2%	87.9%	**<0.001**
Female	87.5%	88.5%	88.1%	**<0.001**
BMI <25 kg/m²	90.3%	88.0%	88.7%	**<0.001**
BMI ≥25 kg/m²	85.7%	86.7%	86.4%	**0.002**
Duration ≤2 weeks	84.6%	85.7%	85.3%	**0.004**
Duration >2 weeks	90.9%	88.9%	89.7%	**<0.001**

Overall, the values of ADA sensitivity and specificity were high in symptomatic patients with tuberculous pleuritis. The p value is statistically significant, suggesting strong association between findings of ADA and the findings of the pleural biopsy. The high negative predictive value indicates that ADA could be particularly beneficial in excluding tuberculous pleural effusions where levels are less than the diagnostic cut-off.

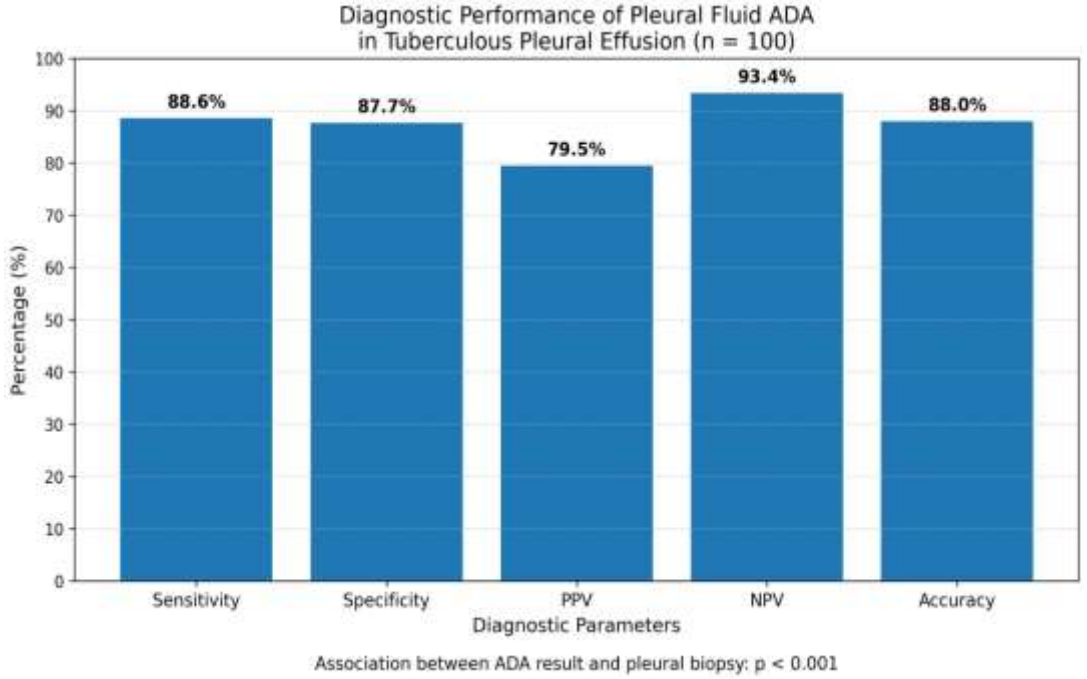

Figure 1. Diagnostic Performance of Pleural Fluid Adenosine Deaminase in Tuberculous Pleural Effusion, Showing Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, and Overall Diagnostic Accuracy. The Association between ADA Result and Pleural Biopsy was Statistically Significant (**$p < 0.001$**).

DISCUSSION

Tuberculous pleural effusion remains an important diagnostic challenge in clinical practice, particularly in areas where tuberculosis is common. Pleural tuberculosis is usually paucibacillary, and direct microbiological confirmation may be difficult in many patients. For this reason, additional diagnostic markers such as pleural fluid adenosine deaminase activity are commonly used to support early diagnosis. In the present study, pleural fluid ADA showed good diagnostic performance for detecting tuberculous pleural effusion among

symptomatic patients, using pleural biopsy as the reference standard (15, 16).

A total of 100 patients who had symptoms of pleural effusion were assessed for this study. The diagnosis of tuberculous pleural effusion was confirmed by pleural biopsy in 35.0% of the patients. When the cut-off value of >55.8 U/L was used, 39.0% of patients had a positive result for ADA. Of the 31 cases that were true positive by ADA, 57 cases were true negative, 8 cases were false positive, and 4 cases were false negative when compared with pleural biopsy. The relationship of the ADA result to the pleural biopsy was statistically significant with a p value of <0.001. This discovery suggests that there is a close association between ADA and tuberculous pleural effusion, a diagnosis confirmed by biopsy (17, 18).

The sensitivity of ADA in the present study was 88.6%, which shows that ADA was able to correctly identify most patients with tuberculous pleural effusion. Specificity was good (87.7%) and ADA also did a good job of excluding non-tuberculous cases. The overall diagnostic accuracy was 88.0%, and the positive predictive value and negative predictive value were 79.5% and 93.4%, respectively. The high negative predictive value is clinically relevant as it means that if patients have ADA levels below the diagnostic threshold, their chance of having tuberculous pleural effusion is low. So, ADA could be particularly useful in the symptomatic patient as a supportive test which is less invasive and can be performed quickly (19).

The results of the present study corroborate the previous studies reporting good diagnostic value of ADA in tuberculous pleural effusion. The usefulness of ADA as a marker was supported by the previous literature, which indicated that it is related to the cellular immune activity, such as activation of T-lymphocytes and macrophages, commonly observed in tuberculous pleuritis. Pleural fluid ADA has been reported to be sensitive and specific, especially in areas where tuberculosis is a common problem. The accuracy of the diagnosis, however, may differ, depending on the cut-off value used, the method of laboratory diagnosis, TB prevalence, and patient selection (20).

Sensitivities and specificities in our study were slightly lower than some reported where values above 90% have been described, but clinically acceptable. This difference could be due to the higher cut-off value used for ADA (55.8 U/L), the severity of the disease, early presentation of some patients, or the presence of non-tuberculous inflammatory pleural diseases. Empyema, inflammatory pleuritis, such as rheumatoid pleuritis, false lymphoma and other inflammatory pleural disorders may cause false positive ADA results. Likewise, false negative results can occur in elderly patients, immunocompromised patients, early stages of disease, and patients with reduced inflammatory responses (21).

Pleural fluid differential cell counts provided additional diagnostic information in the present study. Patients with biopsy-confirmed tuberculous pleural effusion had a significantly higher mean lymphocyte percentage and lymphocyte-to-neutrophil ratio than biopsy-negative patients, whereas their mean neutrophil percentage was significantly lower. Lymphocyte-predominant pleural effusion was also considerably more frequent among biopsy-positive patients. This finding reflects the predominantly cell-mediated immune response associated with tuberculous pleuritis. Therefore, combining pleural fluid ADA with differential leukocyte counts may improve diagnostic confidence, particularly in patients whose ADA levels are close to the selected diagnostic threshold.

The present study also revealed that patients with the duration of pleurisy effusion for more than 2 weeks and patients with a positive family history of tuberculosis were significantly associated with biopsy proven TB. This is consistent with the clinical finding of longer symptoms, in the pleural space, and epidemiological exposure to TB, that are associated with a high incidence of tuberculous pleural effusion. The demographic parameters, age, gender, BMI, place of residence and socioeconomic status, however, did not seem to significantly influence the diagnostic performance of ADA. Stratified analysis also showed good sensitivity, specificity and accuracy of ADA among various patient groups (22).

A strength of this study is that ADA was compared to pleural biopsy which was considered as the gold standard. This helps the accuracy assessment of the diagnosis to be more accurate. The study also involved symptomatic patients from a real clinical setting, and thus the results are applicable in routine clinical practice. If a hospital lacks immediate access to advanced diagnostics (molecular testing or culture), then, an early

prediction for subsequent management may be made using ADA in pleural fluid.

However, some limitations should also be considered. The results are from a single centre and a limited number of patients (100) and therefore may not be applicable to other patient groups. No parallel reference tests were included in the studies of culture, GeneXpert, or other molecular diagnostic tests. Moreover, no assay of ADA isoenzymes was performed which could have further facilitated the interpretation of diagnosis. However, the findings are quite clear that pleural fluid ADA can be a useful diagnostic aid in tuberculous pleural effusion, when used in conjunction with clinical features and findings from pleural biopsy.

Overall, the present study indicates that pleural fluid ADA is a suitable, prompt and lesser invasive diagnostic tool for tuberculous pleural effusion. It cannot completely supplant pleural biopsy in all patients, particularly where there is a suspicion of malignancy or drug-resistant TB, but it can assist the clinician to make timely decisions. In resource limited areas where early diagnosis is critical to minimize delay in treatment, ADA testing may be useful.

CONCLUSION

This study concluded that pleural fluid adenosine deaminase activity showed good diagnostic accuracy for detecting tuberculous pleural effusion among symptomatic patients. At a cut-off value of >55.8 U/L, ADA demonstrated high sensitivity, specificity, negative predictive value, and overall diagnostic accuracy when compared with pleural biopsy. The significant association between ADA and pleural biopsy findings supports the use of ADA as a valuable diagnostic marker.

Patients with biopsy-confirmed tuberculous pleural effusion also showed higher pleural fluid lymphocyte percentages and lymphocyte-to-neutrophil ratios, while lymphocyte-predominant effusion was significantly more frequent in this group. These findings indicate that combining ADA measurement with pleural fluid differential cell counts may further strengthen the diagnosis of tuberculous pleural effusion.

ADA testing is rapid, relatively simple, and less invasive than pleural biopsy. It may therefore be used as an important supportive diagnostic tool, particularly in high tuberculosis-burden and resource-limited settings. However, ADA results should be interpreted together with clinical findings, radiological assessment, pleural fluid cellular patterns, and histopathological or microbiological confirmation where required.

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