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# COMPARING THE EFFECTIVENESS OF ADA/SERUM CRP RATIO, LYMPHOCYTES/NEUTROPHIL RATIO AND ADA IN DIFFERENTIATING TUBERCULOUS PLEURAL EFFUSION FROM EXUDATIVE EFFUSIONS

DR. SAKTHI BHALAN PANDIARAJAN[1],
DR. SACHIN VIDYASAGAR[2], DR. GANGADHARAN VADIVELU[3],
MS PRIYANKA[4] DR.TAMILSELVI R[5]
[1,2,3,4]SAVEETHA MEDICAL COLLEGE
[5]READER, DEPARTMENT OF CONSERVATIVE DENTISTRY & ENDODONTICS, SREE BALAJI DENTAL COLLEGE & HOSPITAL, CHENNAI, INDIA

**Abstract**

**Background:** Tuberculous pleural effusion (TPE) is a frequent cause of exudative pleural effusion in regions with a high tuberculosis burden. Although pleural fluid adenosine deaminase (ADA) remains a key diagnostic tool, its specificity is compromised by elevated levels in other infectious and malignant diseases. Additional parameters, such as the lymphocyte-to-neutrophil (L/N) ratio and the ADA-to-serum C-reactive protein (CRP) ratio, have shown potential in improving diagnostic precision.

**Materials and methods:**A prospective study was carried out in the Department of TB and Respiratory Medicine at Saveetha Medical College and Hospital. Sixty patients above 15 years of age with exudative pleural effusion, confirmed using Light's criteria, were enrolled. Patients with transudative effusions, HIV, malignancy, or age below 15 years were excluded. Clinical assessment, imaging, and laboratory investigations including pleural ADA, L/N ratio, and ADA/CRP ratio were performed. Statistical analysis was conducted using SPSS version 26.

**Results:**Among the participants, 57% were diagnosed with TPE and 43% with non-TB effusions. ADA levels above 40 U/L yielded a sensitivity of 89.35% and specificity of 68.9%. The L/N ratio (>0.75) demonstrated superior performance, with 98.44% sensitivity and 82.70% specificity. The ADA/CRP ratio (>1.25) proved useful in cases with borderline ADA levels. When all three parameters were used together, the diagnostic accuracy reached 100% sensitivity and 85.47% specificity, with a positive predictive value of 89.17% and a negative predictive value of 95.67%.

**Conclusion:**Integrating pleural ADA, L/N ratio, and ADA/CRP ratio offers markedly higher diagnostic accuracy for TPE compared with ADA alone. This combined biomarker strategy may reduce the need for invasive procedures and allow for faster initiation of treatment in high TB-prevalence settings.

**Keywords:**Tuberculous pleural effusion, Adenosine deaminase, Lymphocyte-to-neutrophil ratio, C-reactive protein, Pleural fluid analysis

## INTRODUCTION

Tuberculous pleural effusion (TPE) remains a common cause of exudative pleural effusion, particularly in countries with a high prevalence of tuberculosis [1]. Despite its frequency, diagnosing TPE is often challenging because its clinical and laboratory features can overlap significantly with those seen in other exudative pleural effusions. Accurate and prompt identification of TPE is critical, as the early initiation of anti-tubercular therapy has a profound impact on patient outcomes, reducing morbidity and the risk of long-term complications [2].

One of the most widely used diagnostic markers for TPE is the measurement of adenosine deaminase (ADA) activity in pleural fluid [3]. While ADA is recognized for its high sensitivity as an indicator of TPE, its specificity can be less than ideal, given that elevated ADA levels may be encountered in inflammatory

conditions such as empyema and certain malignancies [4]. This limitation has led researchers to investigate supplementary biomarkers that may provide additional discriminatory power. Among these, the lymphocyte/neutrophil (L/N) ratio in pleural fluid has emerged as a particularly informative parameter, as TPE is generally characterized by a marked lymphocytic predominance [5]. In contrast, effusions of other etiologies often display higher neutrophil counts. Similarly, the ADA/serum C-reactive protein (CRP) ratio has attracted interest due to its ability to integrate indices of local immune activation with systemic inflammatory response, reflecting the complex pathophysiology of tuberculosis in pleural involvement [6].

The aim of the present study is to enhance the diagnostic accuracy for tuberculous pleural effusions by combining pleural ADA, the L/N ratio, and the pleural ADA to serum CRP (pADA/sCRP) ratio.

## MATERIALS AND METHODS

This prospective study was conducted on patients, who presented to the department of TB and respiratory medicine at Saveetha medical college and hospital. After obtaining clearance and approval from the institutional ethics committee,60 patients who met the eligibility criteria were included for the study. Patients were classified as exudative and transudative pleural effusions based on Light's criteria.

**Inclusion criteria**

- All exudative pleural effusion cases are based on Light's criteria.
- Age >15 years.

**Exclusion criteria**

- Patients with transudative pleural effusion
- Patients with immunodeficient states like HIV, those on chemotherapy were excluded.
- Patients with malignant pleural effusion.
- Age < 15 years.

Although 72 cases were taken 12 cases where excluded based on exclusion criteria. Patients above 15 years of age, of either gender, presenting with exudative pleural effusion coming to the TB and chest medicine as outpatients and inpatients was assessed. Besides a detailed history and clinical examination, the following investigations were carried out: Chest imaging - postereolateral view and lateral view (in selected cases), USG chest, Blood investigations: Erythrocyte sedimentation rate, total protein, serum LDH, Sputum examination - for acid fast bacilli by ZeihlNeelsen(ZN) stain, gram's stain, culture and sensitivity, Mantoux's test, Pleural fluid analysis, Serum CRP (S-CRP). The results were tabulated in MS Excel and data analysis was done using SPSS software version 26. Frequencies and percentages was calculated.

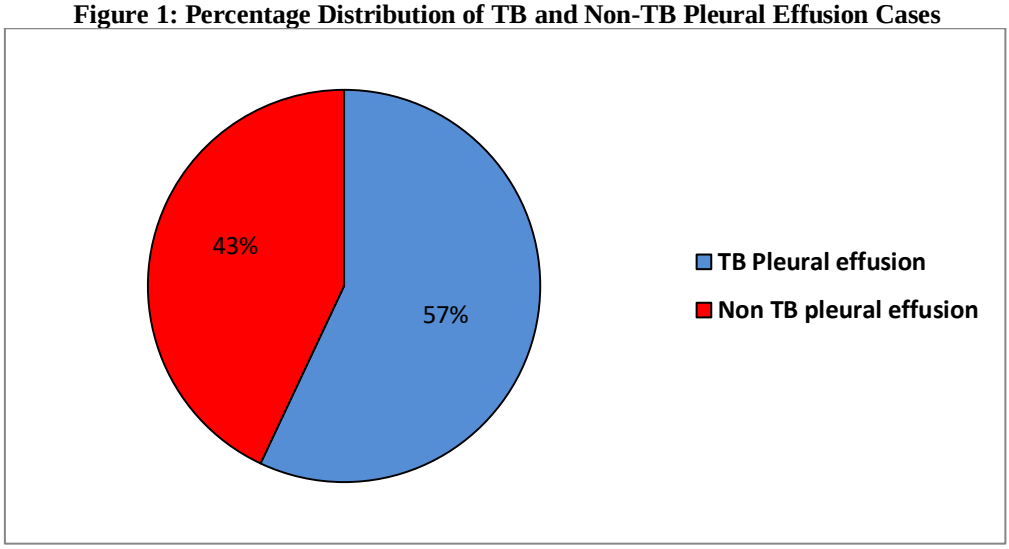
## RESULTS

**Table 1: Demographic Distribution of Study Participants**

| S.No | Variable | Category | Frequency (n) | Percentage (%) |
|---|---|---|---|---|
| 1 | Age (Years) | 15–20 | 2 | 3 |
| | | 21-40 | 17 | 28 |
| | | 41-50 | 11 | 18 |
| | | >50 | 31 | 38 |
| 2 | Gender | Male | 43 | 72 |
| | | Female | 17 | 28 |

The age distribution of participants showed that the majority were aged above 50 years (38%), followed by the 21–40 years group (28%), 41–50 years group (18%), and 15–20 years group (3%). Males constituted 72% of the study population, while females accounted for 28% (Table 1).

**Figure 1: Percentage Distribution of TB and Non-TB Pleural Effusion Cases**




Out of the total cases, 57% were diagnosed with tuberculous pleural effusion and 43% with non-tuberculous pleural effusion (Figure 1).

**Table 2: Distribution of Laboratory Test Results among Study Participants**

| S.No | Test | Result | Frequency (n) | Percentage (%) |
|---|---|---|---|---|
| 1 | AFB Smear | Negative | 41 | 68 |
| | | Positive | 19 | 32 |
| 2 | ESR | Normal | 6 | 10 |
| | | Abnormal | 54 | 90 |
| 3 | C-Reactive protein | Normal | 11 | 18 |
| | | Abnormal | 49 | 82 |
| 4 | Mantoux Test | Normal | 22 | 37 |
| | | Abnormal | 38 | 63 |

The distribution of laboratory test results is shown in Table 2. AFB smear was positive in 32% of patients, while 68% were negative. ESR was elevated in 90% of cases. C-reactive protein (CRP) levels were abnormal in 82% of patients, and the Mantoux test was positive in 63% of cases

**Table 3: Frequency Distribution of ADA in TB and Non-TB Pleural Effusion**

| ADA (U/L) | TB Pleural Effusion | Non-TB Pleural Effusion | Total |
|---|---|---|---|
| >40 | 34 | 14 | 48 |
| <40 | 6 | 6 | 12 |
| **Total** | 40 | 20 | 60 |

**Table 4: Frequency Distribution of ADA / CRP Ratio in TB and Non-TB Pleural Effusion**

| ADA / CRP Ratio | TB Pleural Effusion | Non-TB Pleural Effusion | Total |
|---|---|---|---|
| >1.25 | 16 | 15 | 31 |
| <1.25 | 7 | 22 | 29 |
| **Total** | 23 | 37 | 60 |

Table 3 shows that ADA levels above 40 U/L were found in 34 TB pleural effusion cases and 14 non-TB cases, whereas ADA levels below 40 U/L were observed in 6 TB cases and 6 non-TB cases. The ADA/CRP ratio (Table 4) was greater than 1.25 in 16 TB cases and 15 non-TB cases, while it was below 1.25 in 7 TB cases and 22 non-TB cases.

**Table 5: Frequency Distribution of L/N Ratio in TB and Non-TB Pleural Effusion**

| L/N Ratio | TB Pleural Effusion | Non-TB Pleural Effusion | Total |
|---|---|---|---|
| >0.75 | 39 | 2 | 41 |
| <0.75 | 8 | 11 | 19 |
| **Total** | 47 | 13 | 60 |

The L/N ratio (Table 5) was greater than 0.75 in 39 TB cases compared to only 2 non-TB cases. A ratio less than 0.75 was seen in 8 TB cases and 11 non-TB cases

**Table 6: Comparative Analysis on Sensitivity, Specificity, PPV and NPV based on ADA and L/N Ratio**

| Analysis | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| ADA | 89.35 | 68.9 | 76.5 | 83 |
| L/N Ratio | 98.44 | 82.70 | 82.50 | 90.36 |
| ADA + L/N Ratio + ADA/S CRP Ratio | 100 | 85.47 | 89.17 | 95.67 |

Table 6 shows the comparative diagnostic accuracy. ADA alone had a sensitivity of 89.35% and specificity of 68.9%, while the L/N ratio demonstrated higher sensitivity (98.44%) and specificity (82.70%). The combination of ADA, L/N ratio, and ADA/serum CRP ratio yielded the highest diagnostic accuracy, with 100% sensitivity and 85.47% specificity.

**Table 7: Distribution of Pleural Fluid Analysis**

| Pleural Fluid Analysis | Mean | Median | S.D |
|---|---|---|---|
| TC | 95.31 | 78.1 | 42.8 |
| ADA | 105.6 | 30.5 | 78.6 |
| LDH | 94.8 | 28.8 | 22.34 |
| L/N Ratio | 67.5 | 85 | 33.5 |
| N/L Ratio | 32.4 | 15 | 32.7 |

Table 7 details the pleural fluid biochemical parameters. The mean TC was 95.31 cells/µL, mean ADA level was 105.6 U/L, and mean LDH was 94.8 U/L. The mean L/N ratio was 67.5, whereas the mean neutrophil/lymphocyte (N/L) ratio was 32.4.

## DISCUSSION

This prospective, hospital-based study was undertaken in the Department of TB and Chest Medicine at Saveetha Medical College and Hospital to assess the diagnostic utility of adenosine deaminase (ADA), the ADA-to-serum C-reactive protein (CRP) ratio, and the lymphocyte-to-neutrophil (L/N) ratio in differentiating tuberculous pleural effusion (TPE) from other causes of exudative effusions. A total of 60 eligible patients were included, of whom 57% were diagnosed with TPE.

The cohort showed a male predominance (74%), with the largest proportion in the 51–60-year age group (26%), followed by those aged 41–50 and 61–70 years (18% each). This demographic distribution reflects earlier findings by Porcel et al., who reported a higher incidence of TPE among men and older individuals [2].

ADA is recognised as a valuable biomarker for TPE, given its association with T-lymphocyte activation during Mycobacterium tuberculosis infection [1]. In this study, using a cut-off of 40 U/L, ADA demonstrated a sensitivity of 89.35% and specificity of 68.9%, with positive and negative predictive values of 76.5% and 83%, respectively. These values closely parallel those reported by Liang et al., although cut-off thresholds ranging from 30 to 100 U/L have been documented, depending on methodology, TB prevalence, and population characteristics [4]. The L/N ratio was found to be an even stronger discriminator, with values above 0.75 achieving 98.44% sensitivity and 82.70% specificity. This aligns with previous studies by Antin et al. and Pettersson et al., which indicate that TPE is usually lymphocyte-dominant, whereas other exudates show lower ratios [7,8]. The ADA/CRP ratio (> 1.25) further enhanced diagnostic accuracy, particularly in cases with borderline ADA results, corroborating the observations of Burgess et al. and Rabbi et al. [9,10].

When all three parameters were applied together, the model achieved 100% sensitivity and 85.47% specificity, offering a highly reliable diagnostic strategy. Given that ADA may be elevated in non-tuberculous conditions such as empyema or rheumatoid pleuritis [11], this multi-marker approach can improve specificity and reduce the need for invasive procedures, especially in high TB-burden, resource-limited settings.

## CONCLUSION

In conclusion, this study underscores the enhanced diagnostic accuracy achieved by combining the adenosine deaminase (ADA)/serum C-reactive protein (CRP) ratio with the lymphocyte/neutrophil ratio (LNR) in differentiating tuberculous pleural effusion (TPE) from other exudative effusions. While ADA alone is a useful marker, its efficacy is significantly improved when paired with the LNR, providing superior specificity and sensitivity. This combined approach is particularly valuable in diagnosing TB pleurisy, although it is less effective for distinguishing malignant, para-pneumonic, or para-malignant effusions. The integration of these ratios into clinical practice can streamline the diagnostic process, reduce the need for further invasive procedures, and expedite appropriate treatment, ultimately improving patient outcomes.

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