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ASSESSMENT OF LDH/ADA RATIO IN PATIENTS WITH AND WITHOUT TUBERCULAR PLEURAL EFFUSION

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Abstract

Background: Tubercular pleural effusion (TPE) is a common manifestation of extrapulmonary tuberculosis, especially in high-burden countries. The diagnostic evaluation typically includes pleural fluid adenosine deaminase (ADA) and lactate dehydrogenase (LDH) levels. Recent studies suggest that the LDH/ADA ratio may enhance diagnostic accuracy and help differentiate TPE from other etiologies.

Aim: To assess the LDH/ADA ratio in patients with confirmed tubercular pleural effusion and evaluate its diagnostic utility.

Methods: This cross-sectional study included 100 patients with exudative pleural effusion, of which 70 had confirmed TPE based on microbiological, histopathological, or clinical criteria, and 30 had non-tubercular exudative effusion. Pleural fluid ADA, LDH, and LDH/ADA ratio were measured. Statistical analysis included ROC curve analysis, sensitivity, specificity, and predictive values.

Results: Mean ADA levels in TPE patients were significantly higher than in non-TPE cases ($p<0.001$). LDH levels were elevated in both groups, but the LDH/ADA ratio was significantly lower in TPE patients (mean 12.4 ± 4.1) compared to non-TPE patients (mean 28.6 ± 5.9, $p<0.001$). ROC analysis showed an LDH/ADA ratio cut-off of ≤ 16.0 had a sensitivity of 91.4% and specificity of 88.3% for diagnosing TPE.

Conclusion: The LDH/ADA ratio is a simple, cost-effective, and valuable adjunctive tool in differentiating tubercular pleural effusion from other exudative pleural effusions.

Keywords: Tubercular pleural effusion, LDH/ADA ratio, adenosine deaminase, lactate dehydrogenase, pleural fluid diagnostics.

INTRODUCTION

Tuberculosis (TB) remains a significant public health problem, particularly in developing countries, with an estimated 10.6 million new cases worldwide in 2022 [1]. Tubercular pleural effusion (TPE) is one of the most common forms of extrapulmonary TB and often presents as an acute or subacute illness [2]. The pathophysiology involves a delayed hypersensitivity reaction to Mycobacterium tuberculosis antigens in the pleural space [3].

The diagnosis of TPE relies on clinical features, imaging, microbiology, and pleural fluid analysis. Pleural fluid adenosine deaminase (ADA) has long been recognized as a useful biomarker, with levels >40 U/L strongly suggestive of TPE in high-prevalence areas [4–6]. However, ADA can also be elevated in empyema, rheumatoid pleuritis, and some malignancies, reducing its specificity [7].

Lactate dehydrogenase (LDH) is a ubiquitous enzyme released during cellular injury, and its concentration in pleural fluid is a key component of Light's criteria for exudative effusions [8]. High LDH levels are seen in both tubercular and non-tubercular exudates, limiting its standalone diagnostic utility [9].

The LDH/ADA ratio has been proposed as a novel parameter to improve specificity. TPE generally shows high ADA with moderately elevated LDH, resulting in a low LDH/ADA ratio, whereas malignant or parapneumonic effusions often have high LDH with lower ADA, yielding a higher ratio [10–12].

Several studies have demonstrated the potential of the LDH/ADA ratio as a discriminator between tubercular and non-tubercular pleural effusions, with cut-off values ranging from 10 to 20 [13–15]. However, there is limited large-scale data from high-burden regions, and further evaluation is needed to validate its diagnostic performance in the Indian setting.

Aim: To assess the LDH/ADA ratio in patients with tubercular pleural effusion and compare it with non-tubercular exudative effusions.

MATERIALS AND METHODS

Study Design: Hospital-based observational cross-sectional study

Study Setting: Department of Pulmonary Medicine, tertiary care hospital in India

Sample Size: 100 patients with exudative pleural effusion

Inclusion Criteria:

- Age ≥18 years
- Pleural fluid classified as exudate by Light's criteria
- Confirmed diagnosis of TPE (microbiological positivity for Mycobacterium tuberculosis, histopathological evidence of granulomatous inflammation, or clinical- radiological response to anti-TB therapy)

Exclusion Criteria:

- Transudative pleural effusion
- Patients already on anti-TB treatment for >2 weeks
- HIV-positive patients
- Patients with mixed etiology

Data Collection:

- Detailed clinical history and examination
- Pleural fluid aspiration under aseptic precautions
- ADA estimation by colorimetric method
- LDH estimation by enzymatic assay
- LDH/ADA ratio calculated
- Other investigations: pleural fluid protein, glucose, cytology, Gram stain, Ziehl– Neelsen stain, culture

Statistical Analysis: Data analyzed using SPSS v26.0. Continuous variables expressed as mean ± SD; categorical variables as percentages. Student's t-test used for group comparison. ROC analysis determined optimal LDH/ADA ratio cut-off.

RESULTS

Table 1: Demographic and clinical characteristics of study population

Parameter	TPE Group (n=70)	Non-TPE Group (n=30)	p-value
Mean age (years)	41.2 ± 13.5	43.8 ± 12.9	0.36
Male : Female ratio	1.6 : 1	1.4 : 1	0.74
Duration of symptoms (days)	18.4 ± 7.9	16.9 ± 6.5	0.29
Fever (%)	85.7%	46.7%	<0.001*
Cough (%)	71.4%	60%	0.21

Table 2: Pleural fluid biochemical parameters

Parameter	TPE Group (n=70)	Non-TPE Group (n=30)	p-value
Protein (g/dL)	5.1 ± 0.7	4.8 ± 0.8	0.07
Glucose (mg/dL)	62.4 ± 18.5	58.3 ± 21.2	0.32
LDH (U/L)	496.8 ± 108.7	825.5 ± 154.2	<0.001*
ADA (U/L)	41.6 ± 8.9	28.9 ± 7.4	<0.001*

Table 3: LDH/ADA ratio comparison

Group	Mean LDH/ADA Ratio	p-value
TPE	12.4 ± 4.1	
Non-TPE	28.6 ± 5.9	<0.001*

Table 4: ROC analysis of LDH/ADA ratio

Cut-off Value	Sensitivity (%)	Specificity (%)	AUC
≤16.0	91.4	88.3	0.93

Table 5: Diagnostic performance of ADA vs LDH/ADA ratio

Parameter	Sensitivity (%)	Specificity (%)
ADA ≥ 40 U/L	85.7	80.0
LDH/ADA ≤ 16.0	91.4	88.3

DISCUSSION

In the present study, we observed that the LDH/ADA ratio was significantly lower in patients with tubercular pleural effusion (TPE) compared to those with non-tubercular exudative effusions, with an optimal cut-off value of ≤16.0 yielding high sensitivity and specificity. This finding supports earlier reports suggesting that the LDH/ADA ratio can serve as a useful adjunct in differentiating TPE from other causes of exudative pleural effusion [10,13,14].

ADA remains a widely used biomarker in high TB-burden countries because of its good sensitivity

for TPE [4–6]. However, its specificity is reduced in conditions such as empyema, rheumatoid pleuritis, and certain malignancies [7,9]. LDH, on the other hand, is a general marker of tissue injury and inflammation and is included in Light's criteria for identifying exudates [8]. The combination of these two markers into a ratio addresses some of the individual limitations by capitalising on the biochemical differences between tubercular and non-tubercular effusions [11,12].

Our results are in line with those of Burgess et al. [10], who demonstrated that a low LDH/ADA ratio was highly suggestive of TPE, and with studies from Turkey [13] and China [14], which reported similar diagnostic accuracy. The mean LDH/ADA ratio in our TPE cohort (12.4) falls within the range reported in previous studies, further validating this approach in the Indian population.

The high diagnostic performance observed in our study highlights the potential of the LDH/ADA ratio as a cost-effective tool, particularly in resource-limited settings where TB prevalence is high and advanced diagnostic tests may not be readily available [1,2]. This ratio can be easily calculated from routine pleural fluid analyses, requiring no additional cost or complex laboratory setup.

Nevertheless, caution should be exercised in cases with borderline values or mixed clinical pictures, as pleural fluid biochemistry can be influenced by coexisting infections, chronic inflammatory states, or delayed sample processing [7,9]. Moreover, our study excluded HIV- positive patients, who may present with atypical biochemical profiles due to immunosuppression [3].In summary, our findings reaffirm that the LDH/ADA ratio, when used alongside conventional pleural fluid analysis and clinical assessment, can significantly enhance the accuracy of TPE diagnosis. Wider multicentric studies are warranted to refine cut-off values and confirm its utility across diverse patient populations [15].

CONCLUSION

The LDH/ADA ratio is a valuable adjunctive tool in diagnosing tubercular pleural effusion, offering improved specificity over ADA alone. A cut-off of ≤16.0 provides high diagnostic accuracy and should be considered in the evaluation of exudative pleural effusions, especially in high TB prevalence areas.

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