

A study to evaluate lactate dehydrogenase: adenosine deaminase ratio as a parameter for tubercular and parapneumonic pleural effusion

¹Dr Ankita Singh, Resident, Department of Medicine, S.M.S. Medical College, Jaipur 302004

²Dr Shashi Bhushan Sharma, Assistant Professor, Department of Medicine, S.M.S. Medical College, Jaipur 302004

³Dr Vinay Kumar Meena , Assistant Professor, Department of Medicine, S.M.S. Medical College, Jaipur 302004

⁴Dr Pradeep Mital, Senior Professor, Department of Medicine, S.M.S. Medical College, Jaipur 302004

⁵Dr Sujata Agarwal, Associate Professor, Department of Medicine, S.M.S. Medical College, Jaipur 302004

⁶Dr Jitendra Kumawat, Junior Specialist, Department of Medicine, S.M.S. Medical College, Jaipur 302004

Corresponding Author: Dr Pradeep Mital, Senior Professor, Department of Medicine, S.M.S. Medical College, Jaipur 302004

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Abstract

Background: Tubercular pleural effusion and Parapneumonic Pleural effusion are routinely encountered cases in General medicine ward with former being a very common entity in our Indian population. Pleural fluid examination has a crucial role in approach to final diagnosis. Pleural fluid Adenosine deaminase and Lactate dehydrogenase values are routinely used to differentiate the two, but sometimes, these may vary making it an indecisive condition. Therefore, this study intend to evaluate the Pleural fluid LDH and ADA ratio as a new diagnostic tool to make the clinical decision more aptly.

Methods: A hospital based prospective cross- sectional study was conducted in patients of confirmed TPE (n = 65) and PPE (n = 65) to compare pleural fluid LDH: ADA ratios among these two groups.

Results: The Median values of pleural fluid LDH were 617 IU/L of TPE patients and 355 IU/L of PPE patients. While, median values of ADA in two categories of patients was 66 IU/L in TPE versus 20 IU/L in PPE. The Median value of LDH/ADA ratio of TPE and PPE were 8.61 (range 1.567- 73.466) and 41.36 (range 5.128- 510.923) respectively. There was significance difference between LDH: ADA ratio of TPE and PPE (p-value - <0.001).

Conclusions: The pleural fluid LDH/ADA ratio, which can be determined from routine biochemical analysis is another important parameter to differentiate TPE from PPE. So, this parameter can be introduced to our routine pleural fluid analysis.

Keywords: Tuberculous pleural effusion, Parapneumonic pleural effusion, Lactate dehydrogenase, Adenosine deaminase.

Introduction

Pleural effusion is a common clinical condition with a broad etiology in which excess fluid builds around the lung¹. A thorough history, physical examination, and imaging along with pleural fluid analysis are fundamental to the diagnosis making. Nature of pleural effusion can further be categorized as transudative or exudative based on mechanism of pleural fluid formation and its chemistry using Light's criteria². Subtypes of exudative effusion often seen in clinical practice mainly consist of tubercular or parapneumonic^{3, 4}. Exudative effusion is the result of inflammatory process of pleura and or decreased lymphatic drainage. Tuberculosis (TB) is the leading cause of pleural effusion worldwide⁵. Despite the advances and the fact that nearly all cases can be cured, TB remains one of the world's biggest threats. It affects millions of people each year and is ranked the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV). In 2014, TB killed 1.5 million people (1.1 million HIV-negative and 0.4 million HIV-positive). India has the highest annual incidence of Tuberculosis and is estimated at 1.98 million, one fifth of the global incidence⁶. While parapneumonic effusion is a type of effusion that arises as a result of pneumonia, lung abscess or bronchiectasis. It is very essential to differentiate the two entities as timely management can decrease the morbidity and mortality from the same and reduce the burden on health care resources at the same time.

Biomarkers such as ADA and LDH are commonly used in diagnosis but have their own limitations. Pleural fluid ADA levels are usually raised in TPE with high sensitivity & specificity, but higher ADA levels have also been seen in other diseases involving lung like empyema⁷. Pleural fluid LDH levels may also be

elevated in both Tubercular & Parapneumonic pleural effusions. Assessment of clinical, demographic, pleural fluid cellular and chemical characteristics enables the differential diagnosis to be narrowed but to reach a definitive diagnosis is still challenging.

The ratio of pleural fluid LDH: ADA has not been investigated to differentiate the tuberculous effusion from parapneumonic pleural effusion except in a few recent studies.

Therefore, Pleural fluid Lactate dehydrogenase: Adenosine deaminase ratio has emerged as a new parameter to differentiate the two. In the studies conducted so far, a significantly lower lactate dehydrogenase: adenosine deaminase ratio is found in tubercular pleural effusion compared to parapneumonic effusions.

A very few, retrospective studies from abroad have shown pleural fluid Lactate dehydrogenase: Adenosine deaminase ratio as a superior parameter to differentiate between tubercular and parapneumonic pleural effusion. Thus, we have undertaken this study with an intent to evaluate the new diagnostic tool in the form of pleural fluid LDH to ADA ratio to make the diagnosis of TPE and PPE more effectively in our daily clinical settings.

Methods

A hospital based prospective cross-sectional study was conducted at Medicine department of SMS hospital, Jaipur from June 2019 to December 2020.

Sample size was calculated as 63 subjects for each of the two groups at alpha error 0.05 and power 80% assuming minimum difference of means to be detected in lactate dehydrogenase: adenosine deaminase ratio of tubercular pleural effusion and parapneumonic effusion 50 with 100 standard deviation (SD). So for the study purpose 65 cases of tubercular pleural effusion and 65 cases of parapneumonic pleural effusion were taken.

Inclusion Criteria: Exudative effusions associated with bacterial pneumonia, lung abscesses, bronchiectasis and tuberculosis and those willing to participate in study were enrolled.

Exclusion Criteria: Diagnosed malignant pleural effusion or any other underlying disease.

65 Patients Each of Tubercular Pleural Effusion and Parapneumonic Pleural Effusion were enrolled in this study from as per inclusion and exclusion criteria. The pleural fluid Adenosine deaminase and Lactate dehydrogenase levels were measured by chemiluminescent enzyme immunoassay system and Lactate dehydrogenase: Adenosine deaminase ratio was calculated. All data were entered in the excel sheet and analyzed statistically. A p-values of <0.05 was taken as significant and $P < 0.001$ as highly significant.

Results

In this study, it was observed that mean age of patients of tubercular pleural effusion was less than the mean age of parapneumonic pleural effusion patients, it was $35.90 (\pm 16.2 \text{ SD})$ years in TPE patients compared to $42.05 (\pm 19.50 \text{ SD})$ years in PPE patients as depicted in table 1 and figure 1 & 2. Male preponderance was seen in both the categories of patients of tubercular and parapneumonic pleural effusion. Out of 65 patients of TPE, 42 (64.61%) were males and 23 (35.38%) were females. Among 65 patients of PPE, we found that 39 (60%) were males and 26 (40%) were females as depicted in the table 2. Out of 130 patients of pleural effusion, 65 each of TPE and PPE as per criteria, their pleural fluid ADA value was measured and compared. The mean value of ADA of TPE and PPE came out to be $72.70 (\pm 35.51 \text{ SD})$ IU/L and $22.50 (\pm 15.66 \text{ SD})$ IU/L respectively. The median of two categories of patients was 66 IU/L in TPE and 20 IU/L in PPE. The p-value was calculated to be <0.001 which was statistically significant (table 3 and figure 3). The

Median values of pleural fluid LDH were 617 IU/L of TPE patients and 355 IU/L of PPE patients

The Median value of LDH/ADA ratio of TPE and PPE were 8.61 (range 1.567- 73.466) and 41.36 (range 5.128- 510.923) respectively (table 14). The significance of difference between two median values of TPE and PPE was calculated with p-value <0.001 indicating significant statistical difference in the two values. Figure 19 shows the graphical representation of range of LDH: ADA ratio of TPE and PPE patients.

Discussion

In the present study the maximum prevalence of TPE was in the age group of 15-35 years and majority of individuals were ≤ 55 years of age. The mean age of TPE patients (35.90 ± 16.2 years) was lower than mean age of PPE patients (42.05 ± 19.50 years). These results were consistent with the result of study conducted by Tunn Ren Tay et al⁸. They observed that mean age of TPE patients was lower than mean age of non- TPE patients. Zay Soe et al⁹ in their study observed that mean age of the TPE patients was 42.6 years.

Our present study showed male preponderance both in TPE and PPE patients. Our results were consistent with the results of Zay Soe et al⁹ and Jinling Wang et al¹⁰. In present study the median value of pleural fluid LDH/ADA ratio of patients of TPE and PPE was 8.61 and 41.36 respectively, significant statistical difference (p-value <0.001) was noted. Our results were consistent with the study conducted by Jinling Wang et al¹⁰. They concluded that the pleural fluid LDH: ADA ratio, which can be determined from routine biochemical analysis, is highly predictive of TPE at a cut-off level of 16.20 and LDH/ADA ratio of pleural fluid in TPE was much less than that of PPE patients (medians were 10.88 versus 66.91 respectively). Similarly in the study done by Amandes Beukes et al¹¹ the mean pleural fluid LDH to ADA ratio in TPE patients was lower than

the patients of definitive alternative diagnosis (6.2 versus 34.3) and p-value was <0.001 which was highly significant.

Conclusion

This study concluded that the pleural fluid LDH: ADA ratio of TPE patients is much lower than that of PPE Patients with significant statistical difference.

The study has thus provided evidence that the pleural fluid LDH/ADA ratio is a useful indicator to distinguish TPE from PPE and can be used as a new tool to make diagnosis effectively. Consequently, it may be useful for the early clinical management of patients with pleural effusion in case of diagnostic dilemma as an adjunct to the existing diagnostic modalities.

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Legend Tables

Table 1: Distribution of Pleural effusion patients according to their age

Age groups (Range)	TPE		PPE	
	Number of patients	Percentage (%)	Number of patients	Percentage (%)
15-35 years	31	47.69	29	44.61
36-55 years	26	40.00	14	21.53
>55 years	8	12.30	22	33.84
Total	65	100.00	65	100.00
Mean±SD	35.90±16.2		42.05±19.50	

Table 2: Distribution of patients of TPE and PPE according to gender

Gender	TPE		PPE	
	Number of patients	Percentage (%)	Number of patients	Percentage (%)
Male	42	64.61	39	60.00
Female	23	35.38	26	40.00
Total	65	100.00	65	100.00

Table 3: Comparison of median values of pleural fluid LDH/ADA ratio of TPE and PPE patients.

LDH/ADA Ratio	TPE	PPE	p- value
Median	8.61	41.36	<0.001 (Significant)
Range	1.567 – 73.466	5.128- 510.923	
Standard deviation	9.871	73.368	