Original Paper

# DIAGNOSTIC EVALUATION OF PLEURAL FLUID : THE ROLE OF TOTAL PROTEIN AND LACTIC DEHYDROGENAGE

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**Abstract**

**Pleural effusions are classified into transudates and exudates based on the criteria developed in 1972 by Light's and colleagues. However, their accuracy has not been evaluated in reported setting. In this study, the performance of pleural fluid to serum ratio of total protein (TPR), pleural fluid absolute lactic dehydrogenase (FLDH) level, and fluid to serum ratio of LDH (LDHR) were compared. TPR had been used instead of the absolute value of fluid protein based on the observation that fluid protein is influenced by changes in the concentration of serum protein. However the rationale of using LDHR remains unexplained. This study also measured pleural fluid cholesterol to see whether it improves the classic criteria of Light's and colleagues in diagnostic separation of transudates and exudates or not.**

**Sixty six patients of pleural effusion admitted to Combined Military Hospital (CMH) Dhaka, Bangladesh between 4 May 2003 to 31 December 2004 were included in this study. Out of 66 patients 51 (77%) had exudative and 15 (23%) had transudative pleural effusion. Pleural effusions are termed exudates if the pleural fluid to serum ratio of total protein (TPR) is > 0.5 or the pleural fluid absolute lactic dehydrogenase (FLDH) level is > 200 IU/L or the pleural fluid to serum ratio of LDH ( LDHR) is > 0.6 and transudates if the TPR is < 0.5 or FLDH is < 200 IU/L or LDHR is < 0.6.**

**FLDH appears to be the most accurate measure for the diagnostic separation of transudates and exudates and LDHR has no role in this process. Combined TPR with FLDH improves the diagnostic accuracy of test. This study also observed that pleural fluid cholesterol was high in exudates than in transudates but it conferred no advantage over measurement of Light's criteria. As there are many ways and tests for differentiating pleural effusion into exudates and transudates, this study proposed that the differentiation should be based on TPR and FLDH level**

## Introduction

Pleural effusion develop in thoracic or systemic diseases and basing on their underlying pathophysiology, they are classified into transudates or exudates[1,2]. Currently, the criteria proposed by Light et al in 1972 is the standard method for this discrimination[3]. However in recent years, several reports indicated that these misclassified a number of effusions and that was why several parameters such as the pleural fluid cholesterol level and the pleural fluid to serum cholesterol ratio, pleural fluid to serum bilirubin ratio and pleural fluid to serum cholinesterase ratio have been proposed in segregating the transudates from exudates with more reliably than those of Light's criteria[4-7]. Nevertheless, all these alternative parameters falsely classified some effusions, and their superiority with respect to the Light's criteria is therefore insignificant if not dubious.

It is clinically important to classify pleural fluid into exudates and transudates because this is indicative of underlying pathophysiological process involved. Such distinction allows appropriate investigations to be instigated, enabling better patient management. A recent meta-analysis of study on pleural fluid found that no test was clearly superior in differentiating exudates from transudates[8]. Although paired and triple tests had higher diagnostic accuracies than individual test. Light's criteria have high sensitivity but lower specificity and therefore do not have high diagnostic efficiency[9]. The purpose of our study was to see how far Light's criteria is effective in differentiation exudative from transudative pleural effusions in reported setting. In addition, this study tried to identify an optimum marker combination to differentiate pleural fluid into transudates and exudates by measuring cholesterol concentration in pleural fluid.

## Materials and Methods

This prospective study was carried out at Combined Military Hospital, Dhaka from 4 May 2003 to 31 December 2004. Seventy one patients with pleural effusion were included in this study. However, 3 patients with uncertain diagnosis and 2 with possible multiple causes were excluded from the study. Patients were followed up for at least 3 months or until a final diagnosis was established. Blood and pleural effusion samples were collected and stored and later analyzed for glucose, protein, lactate dehydrogenase (LDH) and cholesterol.

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Pleural fluid were also tested for total cell count, differential cell count, Gram stain, bacterial culture, ZN stain, AFB culture and cytology. Further investigations, such as bronchoscopy and pleural biopsy were performed in whom the aetiology had not been decisive.

**Results**

Of the 66 patients with pleural effusion, 51 (77.27%) were exudates and remaining 15 (22.73%) were transudates. As expected, the TPR, FLDH and LDHR were different in exudates and transudates (Table-I). Fluid TP, TPR and LDH measurement were almost equally good in differentiating between exudates and transudates. Fluid LDH, TPR and TP misclassified 4, 5 and 7 patients respectively out of 66 cases (Table-II). When FLDH and TPR were used in combination, such that an exudate was classified if either of these parameters was found to be positive, then all the 51 patients of exudative nature were classified correctly. The measurement fluid of cholesterol conferred no advantage over measurement of TPR and FLDH values, although fluid cholesterol measurements were better than fluid total protein for classifying exudates (Table II).

**Discussion**

Diagnosis of pleural effusion into transudates and exudates is a useful strategy for evaluating patients with pleural effusion. There is no biochemical marker that allows a complete differentiation between transudates and exudates[1,9]. At most hospitals only fluid total protein is measured routinely to classify the fluid as a transudates or an exudates. This analysis indicates that the pleural fluid absolute LDH level was the most accurate test for the diagnostic separation of pleural effusions into transudates and exudates. This finding is in conformity with the finding of Chandrasekhar et al[10]. This superior performance may be attributed to the increased local generation of LDH in exudative process than the relatively low generation in transudative process[11]. In the diagnostic separation of pleural effusions, the TPR has

**Table-I:** Classification of pleural fluid as per Light's criteria ( n= 66 )

| | No of patients | TPR (average) | FLDH (average) | LDHR (average) |
|---|---|---|---|---|
| Cut off point | -- | >0.5 | 200 IU/L | >0.6 |
| Exudates | 51 | 0.65 | >230 | 0.83 |
| Transudates | 15 | 0.34 | 155 | 0.39 |

**TPR-** Fluid to serum total protein ratio; **FLDH-** Fluid lactate dehydrogenase value; **LDHR-** Fluid to serum LDH ratio.

**Table-II :** Pleural fluid classification into exudates and transudates using clinical diagnosis and by analysis of fluid and serum total protein, LDH and cholesterol (n= 66 )

| Clinical diagnosis | No of patients | Fluid total protein | | Fluid cholesterol | | Fluid LDH | | Fluid:serum total protein | | Fluid LDH+ Fluid:serum total protein | | Light's criteria | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | TP | FN | TP | FN | TP | FN | TP | FN | TP | FN | TP | FN |
| **Exudates** | 51 | 47 | 4 | 48 | 3 | 49 | 2 | 48 | 3 | 51 | 0 | 47 | 4 |
| **Tuberculosis** | 35 | 33 | 2 | 33 | 2 | 34 | 1 | 33 | 2 | 35 | 0 | 33 | 2 |
| **Malignancy** | 10 | 9 | 1 | 9 | 1 | 9 | 1 | 9 | 1 | 10 | 0 | 9 | 1 |
| **Parapneumonia** | 5 | 4 | 1 | 5 | 0 | 5 | 0 | 5 | 0 | 5 | 0 | 4 | 1 |
| **SLE** | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 |
| | | TP | FN | TP | FN | TP | FN | TP | FN | TP | FN | TP | FN |
| **Transudates** | 15 | 12 | 3 | 11 | 4 | 13 | 2 | 13 | 2 | 14 | 1 | 12 | 3 |
| **CCF** | 9 | 7 | 2 | 6 | 3 | 8 | 1 | 7 | 2 | 8 | 1 | 7 | 2 |
| **RF with dialysis** | 3 | 2 | 1 | 2 | 1 | 3 | 0 | 3 | 0 | 3 | 0 | 2 | 1 |
| **NS** | 2 | 2 | 0 | 2 | 0 | 1 | 1 | 2 | 0 | 2 | 0 | 2 | 0 |
| **Cirrhosis** | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 |

CCF - Congestive cardiac failure; RF - Renal failure; NS - Nephrotic syndrome; FN - False Negative; TP - True positive.

been chosen instead of the absolute value of total protein on the assumption that the concentration of total protein in the pleural fluid is influenced by changes in serum protein level. This was also confirmed by reported data which showed that TPR was more sensitive than TP to differentiate exudates from transudates. But this was not significant for correlation between serum and pleural fluid concentration of LDH in exudates and transudates. LDHR was not used for that. Combination of markers gives better result for exudates than transudates which was also reflected in this study.

There are a number of alternative parameters that have been proposed to improve the classic criteria of Light's and colleagues. These nearly developed methods include pleural fluid cholesterol level. However, reported data did not show any significant improvement in diagnostic separation of transudates from exudates by measuring pleural fluid cholesterol level.

## Conclusion

The FLDH is the most accurate test in the diagnostic separation of pleural effusion into transudates and exudates, though the value of FLDH may differ depending on the methodology used for estimation. Combining TPR and FLDH is meaningful as the combination improves the test accuracy. As the pleural fluid concentration of LDH is not influenced by the serum concentration, there is no basis for using LDHR in the diagnostic separation of pleural effusions. As there are many ways and tests for differentiating pleural effusion into exudates and transudates, it is therefore proposed that the diagnostic separation of pleural effusion into transudates and exudates should be based only on TPR and FLDH levels and these criteria were also valid for patients of reported series.

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