

## An Observational Trial Evaluating the Function of Total Protein and Combined Pleural Fluid Cholesterol in the Differentiation of Exudates and Transudates

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### Abstract

**Background:** Light's criteria were the traditional method of distinguishing between exudative and transudative pleural effusions, which wrongly categorizes 15-20% of transudates as exudates. To distinguish between exudative and transudative pleural effusions, the study aims to ascertain the value of combining total protein and cholesterol from pleural fluid.

**Methods:** The study included patients who had pleural effusions. To determine their use in classifying the pleural effusions, the combined pleural fluid cholesterol and total protein were compared with Light's criteria as well as with the discharge diagnosis.

**Results:** Forty-two (51.9%) of the 81 individuals who were enrolled in the trial were men. 11.1% of pleural effusions were determined to be transudates and 88.8% to be exudates using Light's criteria. More pleural fluids were classified as exudates by Light's criteria than under the discharge diagnosis. For the classification of exudative and transudative pleural fluid, 62.9% of 81 samples fell under exudates, and 37.03% under transudates, with a sensitivity of 87.9% and a specificity of 100%, based on pleural fluid cholesterol >60 mg/dL and protein >3 g/dL.

**Conclusion:** Even though Light's criteria are still the gold standard for distinguishing between transudates and exudates, combining pleural fluid cholesterol and total protein produces findings that are almost identical without the need for simultaneous blood tests.

**Keywords:** Exudates; Light's criteria; Pleural effusion; Transudates.

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### Introduction

Fluid enters the pleural space through the interstitial spaces of the lungs, the diaphragm's channels, and the capillaries of the visceral pleura in the parietal pleura. Its elimination is the function of the parietal pleura's lymphatics. The accumulation of pleural fluid occurs when lymphatics are restricted or when pleural fluid production surpasses absorption. The initial step in the diagnosis process is to ascertain if the pleural effusion is exudative or transudative.[1]

With sensitivity and specificity of 99% and 98%, respectively, Light's criteria are more well recognized than any other criteria for distinguishing between transudative and exudative effusion.[2] Light's criteria's primary drawback is that they classify 15-20% of transudative pleural effusions as exudative, particularly in patients with congestive

heart failure taking diuretics.[3] The ability of pleural cholesterol levels to distinguish between exudative and transudative effusions with less misclassification than any of the light's parameters has been investigated.[4] Pleural cholesterol may be a biomarker for distinguishing between exudative and transudative pleural effusions, as several studies indicate that it is elevated in pleural exudates.[4,5]

Pleural cholesterol levels are believed to rise as a result of cellular deterioration (leukocytes and erythrocytes) and vascular leakage brought on by increased permeability.[5] Nevertheless, it appears that higher cholesterol levels in exudative effusions are unrelated to serum levels. A study conducted in India demonstrated 100% sensitivity and specificity when using combined pleural fluid cholesterol and

total protein to distinguish between transudative and exudative effusion.[6]

It is still challenging to distinguish between transudative and exudative pleural effusions using a single parameter. In order to distinguish between transudative and exudative effusions, Light's criteria need measurements of four biochemical parameters, which can be challenging, expensive, and require simultaneous blood samples. Meanwhile, 15–25% of transudative effusions are incorrectly classified as exudates. We investigate if similar outcomes might be achieved utilizing pleural fluid cholesterol and total protein in order to streamline the diagnostic process and eliminate the necessity for simultaneous blood sample. The purpose of this study was to determine the significance of comparing total protein and combined pleural fluid cholesterol with Light's criterion.

### Material and Methods

An observational study was conducted at the medicine department of Darbhanga Medical College and Hospital in Laheriasarai, Bihar, between October 2020 and March 2021.

All patients presenting with sonographic, radiographic, or clinical signs of pleural effusion were included after giving written informed consent. Patients with subsequent pleural effusion from trauma, hydropneumothorax, or refusal to agree were excluded from the study.

Following informed permission, patients with clinical signs and symptoms of pleural effusion who were admitted to the SKMCH medicine wards were assessed and enrolled. Every patient had a chest x-ray taken. When necessary, investigations were conducted, such as a chest USG in the event of a small or suspected pleural effusion on a chest X-ray.

Those patients with pleural effusion had then undergone thoracentesis. 10 ml of pleural fluid was obtained by a disposable plastic syringe maintaining all aseptic precautions in inpatient settings. The sample of pleural fluid thus obtained was sent immediately and those samples not feasible to send immediately to the laboratory for analysis were refrigerated until analysis was done within 24 hours of sample collection. The pleural

fluid was analyzed for total protein, LDH, glucose, TC, DC, malignant cells, ADA, Gram's stain, AFB stain, bacterial culture, and cholesterol level along with simultaneous blood samples for LDH and total protein. A blood sample was also sent for other routine investigations like TC, DC, Hb, ESR, RFT and electrolytes. Other investigations like sputum for AFB, sputum culture, sputum for malignant cell, bilirubin, SGPT, SGOT, ECG, Echocardiography, contrast-enhanced CT of the chest, Bronchoscopy and biopsy, Ultrasound of abdomen and pelvis were done as indicated according to the history and physical examination findings. The final diagnosis was made based on clinical judgment and supportive investigations.

All investigations were recorded in the tabulated proforma. The best cutoff value for pleural fluid cholesterol >60 mg/dL was calculated using the ROC curve with area under the curve (AUC) of 0.968 and sensitivity of 86.9% and zero false-positive rates. Pleural fluid cholesterol >60mg/dL and protein >3g/dL were taken to classify pleural fluid as exudates in this study. It was compared with the diagnosis on discharge. The statistical significance of Light's criteria was measured and compared with the diagnosis on discharge to find out their usefulness in categorizing the pleural effusions. All the data were entered using Microsoft Excel version 2007. Statistical analysis was done using SPSS 20.0. Normally distributed data were expressed as mean± standard deviation and categorical variables as numbers and frequencies. A Chi-square test was used for comparison between the groups.

### Results

This study involved the enrollment of 81 pleural effusion patients. Out of all the participants, 42 (51.9%) were male. The patient was 45.88±18.25 years old on average. The majority of pleural effusion patients are between the ages of 25 and 35. Of the 43 patients who smoked, 25 (58.1%) were men, and 12 (14.8%) also drank alcohol, of whom 8 (66.6%) were men and 4 (33.3%) were women. TB was the most frequent cause of pleural effusion, followed by parapneumonic effusion, malignancy, and dilated cardiomyopathy (DCM). (Table 1)

**Table 1: Major presenting symptoms/signs in different diagnosis on the discharge of the study population**

Diagnosis symptoms/ signs	TB Pleural Effusion (n=37)	DCM (n=18)	Malignancy (n=9)	Parapneumonic Effusion (n=7)	Empyema Thoracic (n=4)	Hepatic Hydrothorax (n=4)	Nephrotic Syndrome (n=1)	Pancreatic Pleural effusion (n=1)
Fever	29(78.3%)	6(33.3%)	1(11.1%)	4(57.1%)	4(100%)	0(0%)	0(0%)	0(0%)
Chest pain	26(70.2%)	8(44.4%)	8(88.9%)	5(71.4%)	4(100%)	4(100%)	0(0%)	1(100%)
Cough	26(70.2%)	14(77.8%)	9(100%)	5(71.4%)	4(100%)	2(50%)	0(0%)	0(0%)
Hemoptysis	2(5.4%)	0(0%)	6(66.6%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Dyspnea	18(48.6%)	18(100%)	5(55.5%)	5(71.4%)	2(50%)	2(50%)	0(0%)	1(100%)
Poor Appetite	2(5.4%)	2(11.1%)	3(33.3%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Weight Loss	2(5.4%)	1(5.5%)	4(44.4%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Edema	1(2.7%)	12(66.6%)	0(0%)	0(0%)	0(0%)	4(100%)	1(100%)	0(0%)
Pallor	0(0%)	0(0%)	3(33.3%)	1(14.2%)	0(0%)	4(100%)	0(0%)	0(0%)
Icterus	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	4(100%)	0(0%)	0(0%)
LN*	0(0%)	0(0%)	4(44.4%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
JVP**	1(2.7%)	7(38.9%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Clubbing	2(5.4%)	0(0%)	5(55.5%)	0(0%)	0(0%)	4(100%)	0(0%)	0(0%)

\*Lymphadenopathy; \*\* Jugular venous pressure

Nephrotic syndrome, pancreatic pleural effusion, hepatic hydrothorax, and empyema thoracic were the least frequent causes. Accordingly, table 1 indicates that fever, chest pain, and cough were the most prevalent symptoms. The sensitivity and specificity of Light's criterion were 96.6% and 30.4%, respectively, with a significant p-value of less than 0.001 and a 95% confidence interval of 0.8 to 0.95. (Table 2)

**Table 2: Relationship between Light's criteria and diagnosis on discharge**

		Diagnosis at discharge		Total
		Exudate	Transudate	
Light's Criteria	Exudate	56(96.6%)	16(69.6%)	72(88.9%)
	Transudate	2(3.4%)	7(30.4%)	9(11.1%)
Total		58(100.0%)	23(100.0%)	81(100.0%)

When the clinical diagnosis of exudative and transudative pleural effusions was compared with pleural fluid cholesterol >60 mg/dL and protein >3 g/dL, 51 out of 58 exudates were correctly categorized, while seven were incorrectly classified

as transudates. Using these standards, all transudates were appropriately categorized. It had a significant p-value of less than 0.001, 95% CI: 0.515-0.734, and sensitivity and specificity of 87.9% and 100%, respectively. (Table 3)

**Table 3: Relationship of Pleural fluid cholesterol and/or protein level with diagnosis on discharge**

		Diagnosis at discharge		Total
		Exudate	Transudate	
Pleural fluid Cholesterol>60mg/dL and Protein >3g/dL	Exudate	51(87.9%)	0(0.0%)	51(62.9%)
	Transudate	7(12.06%)	23(100.0%)	30(37.03%)
Total		58(100.0%)	23(100.0%)	81(100.0%)

**Discussion**

The majority of patients in our study were between the ages of 25 and 35, and the mean age of the pleural effusion patients was 45.88±18.25.

This was comparable to a study conducted by Dhital, K. et al.[7] Liam CK et al.[8] observed that tuberculosis was the most common cause of

exudative pleural effusion, followed by malignancy.

Other studies also indicated that tuberculosis was the most common cause of exudative pleural effusion.[7, 9]Our findings were consistent with those of the previously stated studies. When compared to the diagnosis on the discharge of our investigation, Light's criteria demonstrated 96.6%

sensitivity and 34.4% specificity, correctly classifying 56 out of 58 (96.6%) exudates. Similar to our investigation, a study conducted at Tygerberg Hospital in South Africa[9] found that Light's criteria had a 98% sensitivity. Our study's sensitivity of 98% was close to that of a study conducted by Patel AK et al.[6]

According to a study by Patel AK et al.6, the specificity of comparing pleural fluid cholesterol >60 mg/dL and protein >3 g/dL with the clinical diagnostic to distinguish between exudative and transudative pleural effusion was 100%, which was similar to our findings. The sensitivity (100%) was not constant, though.

### Conclusion

Even though Light's criteria is still the gold standard for differentiating between transudative and exudative pleural effusion, the combination of pleural fluid cholesterol and total protein produces results that are almost identical without the need for contemporaneous blood investigations. Therefore, in settings with limited resources, combined pleural fluid cholesterol and total protein can be used as an alternative to Light's criteria to streamline the diagnosis procedure and eliminate the need for a contemporaneous blood sample. To make definitive conclusions, more extensive research is still needed.

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