

Study on Role of Combined Pleural Fluid Cholesterol and Total Protein in Differentiation of Exudates and Transudates: A Observational Trial**Ranjay¹, Ganesh Paswan², Bhagwan Das³**^{1,2}Senior Resident, Department of Medicine, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar³Professor and Head of Department, Department of Medicine, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar

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Conflict of interest: Nil

Abstract:**Background:** The conventional approach to differentiating between exudative and transudative pleural effusions, which incorrectly classifies 15-20% of transudates as exudates, had been Light's criteria. The purpose of this study is to determine the usefulness of combining total protein and cholesterol from pleural fluid in order to differentiate between exudative and transudative pleural effusions.**Methods:** Patients with pleural effusions were enrolled for the study. The combined pleural fluid cholesterol and total protein were compared with Light's criteria and also compared with the diagnosis on discharge to find out their usefulness in categorizing the pleural effusions.**Results:** A total of 81 patients enrolled in the study, 42 (51.9%) were male. Based on Light's criteria, 88.8% pleural effusions were found to be exudates and 11.1% were found to be transudates. Within the criteria, Light's criteria categorized more pleural fluids as exudates than the diagnosis on discharge. Based on pleural fluid cholesterol >60mg/dL and protein >3g/dL for the classification of exudative and transudative pleural fluid, 62.9% out of 81 samples fell under the exudates and 37.03% pleural effusions under transudates with the sensitivity 87.9% and specificity 100%.**Conclusion:** Combining pleural fluid cholesterol and total protein yields results that are almost similar without the requirement for concurrent blood examinations, even if Light's criteria is still the gold standard for differentiating transudates and exudates.**Keywords:** Exudates; Light's criteria; Pleural effusion; Transudates.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Fluid enters the pleural space via the diaphragm's channels, the visceral pleura's capillaries in the parietal pleura, and the lungs' interstitial spaces. The lymphatics in the parietal pleura are responsible for its removal. When the production of pleural fluid exceeds its absorption or when lymphatics are blocked, pleural fluid builds up. Determining whether the pleural effusion is transudative or exudative is the first stage in the diagnosing process. [1]

Light's criteria have been universally accepted than any other criteria for differentiating transudative and exudative effusion with sensitivity and specificity of 99% and 98% respectively. [2] The main disadvantage of Light's criteria is that they identify 15-20% of transudative as exudative pleural effusions especially in congestive heart failure patients receiving diuretics. [3] Pleural cholesterol levels have been explored for their usefulness in differentiating transudative and exudative effusion with less misclassification than any of the light's param-

eters. [4] Several studies suggest that pleural cholesterol is increased in pleural exudates, making it a potential biomarker for differentiating exudative and transudative pleural effusions. [4,5] Cellular degeneration (leukocytes and erythrocytes) and vascular leakage due to increased permeability are thought to elevate pleural cholesterol levels. [5] However, elevated cholesterol levels in exudative effusions seem to be independent of serum levels. Using combined pleural fluid cholesterol and total protein for differentiation of transudative and exudative effusion, a study done in India, showed sensitivity and specificity of 100%. [6]

Differentiating pleural effusion as transudative or exudative is still difficult using a single criterion. Light's criteria need measurements of 4 biochemical measures for differentiation of transudative and exudative effusions which could be difficult, costly, and need for simultaneous blood sampling at the same time. In the meantime, it misclassifies 15-20% of transudative effusions to exudates. To sim-

plify the diagnostic procedure and omitting the need for simultaneous blood sampling, we examine whether comparable results could be obtained using pleural fluid cholesterol and total protein. This study aimed to compare combined pleural fluid cholesterol and total protein with Light's criteria and find its significance.

Material and Methods

From July 2019 to June 2020, an observational study was carried out at the medical department of Sri Krishna Medical College and Hospital in Muzaffarpur, Bihar. After providing written informed consent, all patients exhibiting clinical, radiographic, or sonographic indications of pleural effusion were included. The study eliminated patients who refused to give consent, had hydro pneumothorax, or had subsequent pleural effusion from trauma.

Patients admitted to the medicine wards of SKMCH with clinical signs and symptoms of pleural effusion were evaluated and enrolled after taking the informed consent. A chest x-ray was performed for each patient. Investigations like USG of the chest in case of minimal or suspected pleural effusion on chest X-ray were done as appropriate.

Those patients with pleural effusion had then undergone thoracentesis. 10ml 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 the 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

A total of 81 patients with pleural effusion were enrolled in this study. There was male predominance with 42 (51.9%) out of total. The mean age of the patient was 45.88±18.25 years. Most patients with pleural effusion belong to the age group of 25-35 years. 43 patients were smokers of which 25 (58.1%) were male. 12 (14.8%) were found to be alcohol consumption, among them, 8(66.6%) were male and 4(33.3%) were female. The most common cause of pleural effusion was tuberculosis, followed by dilated cardiomyopathy (DCM), Malignancy, and Parapneumonic effusion. (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

The least common causes included were Empyema thoracic, hepatic hydrothorax, Nephrotic syndrome, and pancreatic pleural effusion. Such wise, fever, chest pain, cough were the most common signs and symptoms as shown in table1. Light's criterion had sensitivity and specificity of 96.6% and 30.4% respectively with a significant p-value of <0.001, 95% CI: 0.8-0.95. (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%)

Comparing pleural fluid cholesterol >60mg/dL and protein >3g/dL with the clinical diagnosis to differentiate exudative and transudative pleural effusions, it classified 51/ 58 exudates correctly whereas 7 were misclassified as transudates. All transudates were correctly classified by these criteria. It had sensitivity and specificity of 87.9% and 100% respectively with a significant p-value of <0.001, 95% CI: 0.515-0.734. (Table3)

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

Mean age of the patient with pleural effusion in our study was 45.88±18.25 and most patients belong to the age group of 25-35, which was similar to a study done by Dhital, K. et al. [7] The most common cause of exudative pleural effusion was tuberculosis followed by malignancy in a study done by Liam CK et al. [8] Other studies found the most common cause of exudative pleural effusion being tuberculosis. [7,9]

All of the above study findings were similar to the finding of our study. Comparing Light's criteria with the diagnosis on the discharge of our study, it correctly classified 56 out of 58 (96.6%) exudates and it had sensitivity and specificity of 96.6% and 34.4% respectively.

The sensitivity of Light's criteria was 98% with a study done in South Africa Tygerberg Hospital [9] which was comparable to our study. The result of a study done by Patel AK et al [6] was also comparable to our study with a sensitivity of 98%.

The specificity of comparing pleural fluid cholesterol >60mg/dL and protein >3g/dL with the clinical diagnosis to differentiate exudative and transudative pleural effusion, a study done by Patel AK et al [6] was 100%, which was comparable to our study. However, the sensitivity (100%) was inconsistent.

Conclusion

The combination of pleural fluid cholesterol and total protein yields results that are almost similar without the requirement for concurrent blood examinations, even if Light's criteria is still the gold standard for distinguishing between transudative and exudative pleural effusion.

Therefore, combined pleural fluid cholesterol and total protein can be utilized as an alternative to Light's criteria in resource-limited settings to avoid the necessity for simultaneous blood sample and simplify the diagnosis process. Larger research is yet required to draw firm conclusions.

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